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TWENTY YEARS' EXPERIENCE WITH THE SURGERY OF HYPERTENSION*

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IN November, 1933, Max M. Peet[1] performed his first splanchnic section for hypertension. The patient was an extremely sick twenty-nine-year-old man, whose blood pressure did not drop below 260 systolic, 150 diastolic, even on bed rest. He was almost blind from hemorrhages and exudates and showed papilledema of 4 diopters. After the operation, however, the blood pressure fell to normal, and he was able to work for ten years, his vision being good enough to enable him to use a micrometer screw.

When I first operated on a patient for hypertension a few months later, a thrombosis of the conus medullaris resulted, followed by incontinence of bladder and bowel. The patient's blood pressure did not drop, nor was his headache relieved.

Neither of these cases presents a true picture of the surgical treatment of hypertension; they represent, rather, extremes. Both of them, however, must have colored the views of the referring physicians.

There is little doubt that the popularity of the operative treatment of hypertension has waned in most sections of the country, and there are at least three reasons for this. The first is that, all in all, a significant reduction in blood pressure is obtained in less than 50 per cent of the patients operated upon. Secondly, convalescence from this operation is a painful one, and the patient may not recover from the more extensive procedures within a year's time. Thirdly, the new hypotensive drugs are in a phase of great popularity, though at present this popularity seems also to be decreasing. It is highly probable that new drugs will be developed that will ultimately replace surgery, but, as yet, this is far from true. I believe that the present trend away from the operative treatment of severe hypertension is illogical, in the light of present knowledge.

Of the first 4 patients operated on by Peet for hypertension, 3 responded favorably. By the time 60 had undergone the procedure, however, it was obvious that the operation was effective in lowering the blood pressure in less than 50 per cent of the cases. Several facts had, by this time, become apparent.

In the first place, when nitrogen retention was present in a well hydrated patient, as judged by an accurate measurement of nonprotein nitrogen, the operation was invariably unsuccessful.

Secondly, it had previously been taught that in essential hypertension, high blood pressure was compensatory, forcing the blood through a narrowed arterial system and, hence, that lowering the blood pressure might be dangerous. This concept was challenged by the very first patient operated upon when the arterial pressure fell from 260 systolic, 150 diastolic, to normotensive levels. In practically every bilateral splanchnic section properly performed, the pressure falls to low levels during the first twenty-four hours, as a result of anesthesia as well as the splanchnic section, although thrombosis of any type has rarely occurred during these hypotensive episodes. This proves beyond question that, even in patients with severe atherosclerosis, hypertension is not necessary to maintain life.

Before long it was concluded that in cases that responded spectacularly to operation, the abnormal arterial process might be reversible because the factor of work hypertrophy was removed from the media or a humoral mechanism altered, or both. It was not realized at that time, however, that the process of intimal change — that is, of atherosclerosis, might be reversible, up to a point at least, if the chemical constituents of the body were in some way changed by operation. The evidence that atherosclerosis is reversible is interesting but still far from convincing. From the funduscopic picture of hypertensive patients, at least, there is no evidence that atherosclerosis can regress. Spasm, hemorrhages, exudates and papilledema frequently disappear after splanchnic section, but even with patients who have maintained a normal blood pressure for some time after operation, there is never a change for the better in the retinal vessels themselves.

I now believe that in many of the cases that do not respond to operation, the arterial process may actually be a primary disease, probably chemical in

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nature. It is believed that individual patients differ genetically in their tendency to become atherosclerotic and that there are many other variables in the symptom complex known as essential hypertension. This is probably the reason why the response to operation varies so greatly from patient to patient.

No criteria have yet been found that make the surgeon confident that a given patient will respond favorably to operation. Recently, 60 patients showing definite blood-pressure reduction at least a year after sympathectomy were carefully studied by Hoobler et al.[2] in the Cardiovascular Laboratory of the University of Michigan in an attempt to find some common denominator that might ensure a good result from operation. These 60 cases were compared with 71 in which death or no significant reduction in blood pressure had occurred. Disappointingly enough, there was no significant difference in the two groups so far as age, known duration of hypertension, cold-pressor test or response to various drugs such as tetraethylammonium chloride was concerned. This lack of difference in postoperative results in patients up to fifty years of age and with hypertension of known duration has been noted by others. Therefore, we are not yet prepared to advise early operation to prevent a theoretically more severe hypertension in the future though it appears, at first glance, to be a logical procedure. I agree with the following statement of Evans and Bartels[3]:

> We are loath to consider this type of operation [lumbodorsal sympathectomy] with its prolonged uncomfortable convalescence as a prophylactic operation for benign hypertension but urge it on patients under 50 years of age with spastic, exudative and hemorrhagic retinal arteriolar changes, moderate cardiac damage, signs of early nephrosclerosis, and labile blood pressure.

It is extremely difficult to compare the results of operation reported from different clinics. I have even found it most difficult to compare follow-up studies from our own clinic. The percentage of what are considered to have been good results has varied considerably in past series, so that I do not know which one of these series can be compared with the most recent statistics. Craig[4] has stated that he has encountered the same difficulty.

There are various reasons for this predicament. Blood pressure fluctuates considerably in the earlier stages of hypertension. There are all sorts of intangibles such as the mood of the patient, the effect and approach of the physician and even the climatic conditions of a particular day. There is also the important factor of the amount of rest the patient has had and his position while the blood pressure was being taken. When, in addition, one considers the fact that a new criterion has been established for the taking of the diastolic pressure (as advised by the American Heart Association), one is forced to wonder how to get from the record a preoperative blood-pressure value that can be compared with the postoperative one.

For these reasons, in the series discussed below, a simpler method than any used in the past was selected though it is admittedly far from foolproof. I have gone over the cases with one of the residents, Dr. John Tytus. We averaged the casual preoperative pressures to the best of our ability. We then compared this figure with that sent in five to eight years postoperatively by the patient's physician, though a few records were made in the Cardiovascular Laboratory. All the patients selected for this series were operated upon by Dr. Peet, in the hope that the subconscious desire to obtain good results that is so difficult for the surgeon to escape would thus be minimized. Each case was a supradiaphragmatic splanchnic section in which the dissection was carried from the twelfth dorsal to, or above, the sixth dorsal ganglion, along with excision of long segments of the splanchnic nerves.

If the diastolic pressure had fallen 20 points the result was usually called good. An exception to this rule was when the diastolic pressure still remained above 120; in such cases the result was considered to be poor. A pressure that had fallen to, or below, 140 systolic, 90 diastolic, was regarded as normal. This does not necessarily mean that the diastolic pressure in such cases had fallen 20 points. In a patient close to fifty years of age at the time of the checkup a level of 150 systolic, 90 diastolic, was considered to be normal. The object of this study was to ascertain whether carrying the dissection higher, as was done after 1946, improved the results or made them comparable to those of the more radical two-stage procedures.

The present study consists of the 268 cases in which the dissection was carried from the twelfth dorsal to, or above, the sixth dorsal segment as a one-stage procedure. These operations were performed from the beginning of 1946 to March, 1949. The operative mortality in this high bilateral resection was 3 per cent. This was actually less than that in the first 1000 consecutive patients (3.5 per cent), in whom the dissection was carried only to the ninth dorsal segment. Sixty-five per cent of the cases were considered to be in Keith–Wagener[5] Groups 3 and 4, though this classification is notoriously inaccurate (unless made by a single observer).

Removal of the twelfth dorsal through, or above, the seventh dorsal segment after resection of only the eleventh rib is a technically difficult procedure. The residents can accomplish this, however, by resection of portions of the tenth and eleventh or the ninth and tenth ribs. Because of the increased danger of surgical shock in such operations 500 cc. of blood is now given routinely. Formerly, transfusion in any splanchnic section was rarely needed.

We cannot compare the results of the present study (Table 1) with those previously carried out in the Clinic because of the different criteria used in the past and the difference in length of follow-up period.

It is known for certain, however, that the results of this latest study are superior to those obtained by the neurosurgical staff in general when radical dissection was not carried out.

Since so much difficulty has been encountered in the evaluation of these results, it can be argued that it would be even more difficult to compare them with those from another clinic. Survival after different procedures can be compared, however, provided the cases are in general of equal severity and also that the same postoperative period is employed and that proportional numbers of men and women are selected.

By far the best controlled series, and one that approaches the ideal, is that of White, Dimond and Williams,[6] though the number of cases reported is relatively small. One hundred patients were selected from the private practice of White, and all were checked preoperatively and postoperatively by him. Each of the patients had "important cardiovascular complications." Fifty were operated on by one surgeon, Smithwick. A medically treated control group of 50 patients observed at about the same time by White was comparable in age, sex and severity of cardiovascular complications.

In the sympathectomized series there were 38 men and 12 women. In White's opinion 44 per cent of these showed definite improvement three to seven years after operation; 24 per cent were dead by the end of this time. In the control group there were 37 men and 13 women. Only 10 per cent of those medically treated showed definite improvement, whereas 82 per cent were dead at the end of seven years.

TABLE 1. *Effect of Removal of the Twelfth Dorsal through, or above, the Seventh Dorsal Segment (Peet) in 241 Patients Adequately Followed for Five to Eight Years.**

RESULT	NO. OF PATIENTS
Good	101 (55% of living & 42% of living & dead)
Excellent (normal blood pressure)	33 (18% of living & 14% of living & dead)

*57 patients died in this period.

In Smithwick's[7] own series of 1266 cases treated surgically (47 per cent men and 53 per cent women), 19 per cent were dead at the end of five years. In what he considers a comparable control series of medically treated patients, 54 per cent were dead at the end of five years. In the control series, however, there were 61 per cent men and 39 per cent women. Since it is well known that men cannot tolerate hypertension as well as women, the comparison of Smithwick's two series is open to some criticism.

In Peet's most recent series of 268 cases, in which 46 per cent were men and 54 per cent women, 22 per cent were dead five to eight years after operation (Table 2). This percentage compares favorably with that of Smithwick, whose figures were taken precisely at the end of five years (Tables 3 and 4). In Peet's[8] series of 1000 patients with less radical operations ten to twenty years ago, 59 per cent are dead. Fifty-three per cent of the patients were women, and 47 per cent were men, exactly as in Smithwick's surgical series. Seventy-five per cent of

TABLE 2. *Effect of Sympathectomy from the Seventh Dorsal (or Higher) through the Twelfth Dorsal Segment on the Survival of 268 Patients Operated on by Peet.*

RESULT	NUMBER	PERCENTAGE
Traced cases	257	96
Deaths	57*	22
Survival	200	78

*Operative mortality, 3%.

all the men, but only 45 per cent of the women are dead. The ability of women to tolerate hypertension better than men has been noted by many observers since Blackford, Bowers and Baker[9] first called attention to it in 1930. It would probably be better if survival studies were compared only in men in the evaluation of the results of various medical and surgical procedures, since women often tolerate a high blood pressure for years.

When patients with severe headache are subjected to splanchnic section, the headache almost invariably disappears even when the blood pressure is not lowered. Patients with severe symptoms that do not respond to medical therapy are consequently preferred as candidates for operation since great symptomatic relief is so often achieved. Asymptomatic hypertensive patients whose blood pressure does not drop after operation are scarcely grateful patients;

TABLE 3. *Effect of Sympathectomy on Survival As Reported in Various Series.*

AUTHOR	YEAR	NO. OF CASES	FOLLOW-UP PERIOD	DEATHS	
				NUMBER	PERCENTAGE
			yr.		
Craig[10]	1949	130	5	11	8
Grimson[11]	1953	110	5-13 10-13	22	16 44
Smithwick[7]	1953	1266* 467†	5 5	241 251	19 54
Peet[8]	1954	257‡	5-8	57	22
White et al.[6]	1950	50* 50†	3-7 3-7	12§ 41§	24 82

*Surgical.
†Medical.
‡7th through 12th dorsal segment.
§All patients had cardiovascular complications.

they do not appreciate being told that, statistically, they should live longer than they would have if they had not been operated upon. It is difficult for them to derive much comfort from statistics while still suffering postoperative pain, especially when they felt fine

before the operation. Nevertheless, if the blood pressure is extremely high, or is tending to climb, especially in a man, and if it does not respond to any form of medical treatment, operation should be advised. I do not hesitate to operate on patients between the ages of fifty and fifty-five if their symptoms are severe.

The morbidity in supradiaphragmatic splanchnic section is less than that in lumbodorsal or "total sympathectomy." Moreover, a one-stage operation is always more acceptable to the patient than a procedure of two or three stages.

TABLE 4. *Effect of Sympathectomy on Blood Pressure.*

AUTHOR	NO. OF CASES	FOLLOW-UP PERIOD	GOOD RESULTS	AUTHOR'S ASSESSMENT
		yr.		
Craig[4] (after 1949)	100	5	51%	"Good Results"
Grimson[11] (1953)	172	Recent to 13	64% living patients 52% living & dead patients	"Significant Reduction"
Peet[3] (1954)	241	5-8	55% living patients 42% living & dead patients	"20 mm. or more fall in diast. BP"
Poppen (Evans & Bartels,[1] 1949)	173	½-2¾	47% of living & dead patients	"50 systolic 20 mm. or more fall in diastolic"
Ray[14] (1949)	291	1-6	60% living & dead patients	"Normal to significant reduction"
Smithwick[7] (1953)	1266	1-5	45% living patients	"Significant Reduction"

It is still not proved that for a maximum lowering of blood pressure it is necessary to carry the dissection below the diaphragm to remove lumbar ganglions. Craig,[10] Grimson et al.[11] and Poppen[12] believe that by carrying their dissections higher they have improved their results, though they continue to excise lumbar ganglions. Ray[13] believes that "there may actually be a little advantage" in the removal of lumbar ganglions, and since, in his experience, the additional procedure necessary to remove lumbar ganglions has not increased the mortality, he is continuing to follow this procedure.

Ray and Neill[15] stimulated the renal artery, vein and renal pelvis in 2 patients undergoing thoracolumbar sympathectomy under local anesthesia. The pain produced by stimulation was obliterated when the greater and lesser splanchnic nerves were divided along with resection of the ganglionated chain from the seventh through the eleventh thoracic segment. It is well known that with peripheral nerves the sympathetic fibers mediating sweat secretion are distributed in the same skin pattern as the sensory fibers. It is possible, then, that the efferent sympathetic fibers entering the kidney, which are capable of producing renal vasoconstriction, enter with the sensory fibers and do not come in below the eleventh dorsal ganglions. More such experiments at the operating table would be interesting and might produce evidence that dissection below the diaphragm is not necessary.

Postural hypotension is quite likely to follow lumbodorsal but is rarely seen after supradiaphragmatic sympathectomy. Some believe that postural hypotension is instrumental in improving survival statistics. This is not borne out by the fact that there is no significant difference between survival statistics in Peet's most recent series and that of Smithwick.

Grimson[11] has been carrying out what amounts to almost total sympathectomy. Sixty-four per cent of 140 living patients have shown significant reduction in blood pressure. These results are somewhat better than those in any other large series reported, and I agree that "total sympathectomy" is more likely to reduce blood pressure significantly than any other procedure carried out on the sympathetic nervous system. I believe, however, that this operation is, as a rule, too high a price to pay for the increased percentage of good results that may be expected from it. For example, more than half these patients have required some form of treatment for the improvement of the nasal airway.

Ray[14] has performed 30 total sympathectomies and has compared them with his much larger series of the lumbodorsal procedure. It is his opinion that the percentage of improved results in the blood-pressure-lowering effect of "total sympathectomy" is hardly great enough to justify the somewhat greater morbidity and mortality that attend total sympathectomy when compared with a less radical operation. Smithwick[7] is in agreement with Ray in this respect. There are advantages to "total sympathectomy," however, in that it deafferentates and decelerates the heart, so that there are definite indications for its use, such as angina pectoris, tachycardia and vasospastic states of the upper extremities.

I mention adrenal resection with sympathectomy chiefly to condemn it, though perhaps this judgment is a bit premature. The results presented by Jeffers et al.[16] are no better so far than those reported by some of the other surgeons mentioned above. As soon as the substance of the remaining adrenal gland functions or hypertrophies, so that replacement therapy is no longer necessary, the effect of adrenal resection no longer operates.

Some discussion of experiences with splanchnic section may be worth while. In 1936 I operated on a hypertensive patient with a known duodenal ulcer. Three different x-ray studies had previously demonstrated activity of the ulcer, with crater formation; after weeks of diet therapy the pain from the ulcer was still uncontrolled. For almost three months after bilateral splanchnic section with excision of the tenth through the twelfth dorsal ganglion all symptoms of ulcer disappeared. X-ray study at this time showed striking improvement in the previously demonstrated lesion. The following statement was made by the X-Ray Department: "Unquestioned improvement in

filling of the duodenal bulb, with relative relaxation of the pyloric sphincter. No identifiable ulcer at this time."

A few days after this last x-ray examination, when I was waxing enthusiastic about this case and considering the extension of the operation of splanchnic section to include duodenal ulcer, the patient showed symptoms of massive concealed hemorrhage. A laparotomy revealed an enormous crater, which had extended into the pancreas. The point of arterial hemorrhage was actually identified. I then realized that in this case the sensory nerve supply to the upper gastrointestinal tract had been sectioned, and that though this patient still had active ulceration, he did not experience pain. The improved x-ray picture may have resulted from the breaking of a reflex arc after removal of the sensory side of this arc.

One must therefore be cautious in performing splanchnic section on patients with ulcer or severe gall-bladder disease. Ray and Neill[15] have demonstrated conclusively that the sensory supply to the gall bladder, pancreas and stomach is by way of the splanchnic nerves and lower dorsal sympathetic chain. Regeneration of these nerves can take place at a later date, but one must remember that patients who have had prior visceral disease, and who have undergone splanchnic section, should receive careful postoperative observation.

Another complication of supradiaphragmatic splanchnic section is chylothorax, about 8 cases of which have occurred among approximately 2500 patients subjected to the operation. In 2 other cases it was possible to secure the duct when it was divided, by means of silver clips, thus obviating chylothorax. These 2 patients did extremely well for some years as far as their hypertension was concerned. In 1941, I operated upon a patient who had previously been in cardiac failure. I experienced considerable technical difficulty and, in the operative note, recorded that a satisfactory excision of the lower sympathetic chain on one side had not been obtained. The patient improved for two years; then his hypertension returned. In view of the history and the operative note, he was operated on again by Dr. Peet, who encountered considerable scarring at the operative site. He removed more of the sympathetic structures, but certainly did not go higher than the ninth dorsal ganglion on one side and the tenth dorsal ganglion on the other. A chylothorax developed, which was later closed. This patient has been followed closely for ten years and is alive and working today. Though he has been in and out of cardiac failure, he has never shown any elevation of blood pressure. It seemed to me that this could not have resulted from a slightly more extensive sympathectomy than was performed at the first operation. It suggested that ligation of the thoracic duct had some effect on this remarkable result. Several other cases of more recent date have shown thoracic-duct fistulas that subsided spontaneously, and, when examined postoperatively, the patients were found to have done well as far as blood pressure was concerned.

All surgeons are familiar with the recent attempts to prevent atherosclerosis by eliminating certain lipids from the diet. Accordingly, three years ago, Parker, Kahn and Iob[17] purposely attempted ligation of the thoracic duct in 10 patients during the operation of splanchnic section, on the theory that when the main thoracic duct was ligated, absorbed fat, instead of reaching the systemic circulation directly, might be subject to modification in the liver if collaterals emptied into the portal system. Careful preoperative and postoperative fat-absorption studies were carried out by Parker and Iob. From anatomic studies we had reason to believe that the main thoracic duct was ligated close to the diaphragm in 7 of these cases. No patients had chylothorax, nor was there evidence of any alteration in fat transport. To our disappointment, there has been no more clinical improvement in these patients than might have been expected from the concomitant splanchnic section. The probabilities are that there are many collaterals between the lacteals and the general circulation that go into action when the main thoracic duct is tied off. Whether atherosclerosis can ever be prevented surgically remains to be seen. We have no evidence, however, that ligation of the main thoracic duct will accomplish this end.

Conclusions

Sympathectomy, followed by a medical regimen such as a salt-free diet, if necessary, is at present the most successful treatment for severe or progressive hypertension of unknown origin.

The operation should never be performed when there is evidence of renal failure as shown by an accurate determination of nonprotein nitrogen of the blood or blood urea nitrogen.

The standard procedures of today all have merit, and the surgeon should employ the one in which he has been trained, or that best suits the individual needs of the patient.

It is regretted that a procedure that has been proved by highly competent surgeons to improve life expectancy in severely ill, hypertensive patients has not been accepted by the majority of practicing physicians.

I wish to express my appreciation to Dr. John S. Tytus, senior resident in Neurosurgery, Mrs. Jean Waters and Mrs. Marian Wortley of the Follow-up Unit in the Record Department for obtaining a 96 per cent follow-up in this series of 268 patients.

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ELECTROENCEPHALOGRAPHIC ABNORMALITIES IN ENDOCRINE DISEASE*

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THE intimate metabolic processes of the brain are closely related to the general metabolism of the body, and the electric activity of the brain varies with certain endocrine functions. Lindsley and Rubenstein[1] showed a correlation between the alpha frequency and the metabolic rate. Gibbs and Gibbs[2] demonstrated changes in the cortical frequency spectrum with the level of thyroid function. Ross and Schwab[3] report that when the alpha rhythm is taken during a "basal state" (with the patient fasting and resting for half an hour) the correlation is not so good as when the patient is well fed, satisfied and relaxed. Brain-wave abnormalities (fast activity, simple spikes and slowing) have been reported in parathyroid insufficiency by Odoriz et al.[4] Greenblatt, Murray and Root[5] described brain-wave changes in diabetic patients, and these were confirmed by Fabrykant,[6] who reported on a group of 15 labile diabetic patients. Electroencephalographic abnormalities were recorded in 80 per cent, and severely disordered patterns consistent with convulsive tendency or focal pathology in almost 50 per cent of the patients.

Islet-cell adenomas may produce extreme electroencephalographic abnormalities as shown by Hoefer, Guttman and Sands,[7] who reported high-voltage slow waves, with frequencies of 2 or 3 per second, and spike-dome formations. Generalized slowing, with some focal slowing, was observed in a case of islet-cell adenoma of the pancreas by Wyke.[8] The slow activity commonly encountered in Addison's disease was shown by Hoffman, Lewis and Thorn[9] to be related to changes in the level of adrenocortical function. Further studies on this subject were conducted by Engel and Margolin,[10] who reported diffuse slow activity with frequencies of 2 to 6 per second but no cortical focus. In normal women the electric activity of the brain often undergoes minor alterations with the onset of the menstrual flow, as demonstrated by Dusser de Barenne and Gibbs.[11] But in the menopause, even with large doses of stilbestrol, Cress and Greenblatt[12] were unable to produce significant changes in the electroencephalogram.

The fact that the electroencephalogram becomes abnormal in many endocrine disorders suggested that it would be profitable to include this procedure in the study of patients with endocrine disturbances.

METHOD

A special sub-laboratory was established and a Grass 8-channel electroencephalograph was installed on the Medical Service of the Veterans Administration Hospital, Hines, Illinois, where patients with metabolic disturbances were studied. Tracings were taken during waking and sleep on 87 patients. Chloral hydrate was used to induce sleep that could not be obtained spontaneously.

Ten solder-disk electrodes coated on their undersurface with bentonite paste were glued to the scalp with collodion. The scalp electrodes were located over the left and right frontal, anterior temporal, temporal, parietal and occipital areas. Recordings were monopolar and bipolar. Reference electrodes were placed on the lobes of both ears; these were used separately or together. For a certain portion of each tracing one of the scalp leads was selected as a reference.

The following cases are illustrative of the diseases concerned.

Hyperthyroidism

A 28-year-old truck helper had been well until 2 years before admission, when he first noted exertional dyspnea. Six months before admission there was a gradual increase in exophthalmos. He was bothered by palpitation, perspiration, heat intolerance and increasing nervousness. He observed fullness and later a definite swelling in his neck. He estimated his weight loss at 25 pounds in spite of a good appetite. He was restless, and his skin flushed and moist.

Physical examination showed severe exophthalmos, with lid lag and difficulty in convergence. The thyroid gland was diffusely enlarged bilaterally to nearly the size of a hen's egg.

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The lungs were normal on auscultation and percussion. The heart revealed normal findings except for tachycardia.

The blood pressure was 140/90, and the pulse 126.

Urinalysis was repeatedly normal. Repeated red-cell counts showed no substantial variation from 4,800,000, with a hemoglobin of 14.5 gm. per 100 cc. White-cell counts ranged between 5000 and 9900, with some increase in lymphocytes. The blood Kahn reaction was negative. The serum calcium was 11.2 mg., the serum inorganic phosphorus 4.0 mg., and the serum cholesterol 184 mg. per 100 cc. Three determinations of the basal metabolic rate were +74, +75 and +70 per cent. Study of radioactive iodine demonstrated 85 per cent uptake, with a protein-bound iodine of 0.209 microgm. per cubic centimeter. X-ray examination of the chest was negative. An electrocardiogram disclosed a sinus tachycardia.

Two electroencephalograms taken before therapy showed exceedingly abnormal patterns, consisting of slow waves (frequencies of 4 to 6 per second) in all leads, large spikes, spikes and irregular domes and runs of fast (25 to 30 per second) waves (Fig. 1). The patient was treated with radioactive iodine and cortisone, and electroencephalograms taken 13, 35 and 60 days later revealed minimal improvement in the 1st, moderate improvement in the 2d and great improvement in the 3d tracing, which showed high-voltage activity, a frequency of 10 per second and a few "spike-like" waves, and which was considered only slightly abnormal. This series of tracings demonstrated that the electroencephalographic improvement paralleled the clinical response to treatment (Fig. 1).

Islet-Cell Adenoma of the Pancreas

This patient entered the hospital with a complaint of convulsions and "memory lapses" occurring about once a month. He was symptom free in the interval between attacks. The memory lapses consisted of 2 to 5 hours of increasing confusion ending in unconsciousness and usually associated with a convulsion and coma.

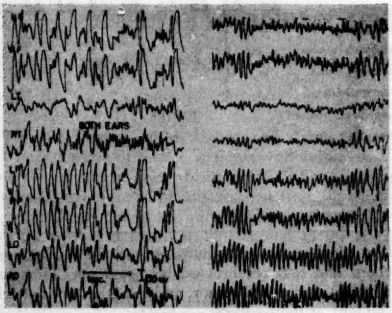

FIGURE 1. *Electroencephalograms in a Patient with Hyperthyroidism.*

A=*strikingly abnormal tracing, with generalized slowing and spike and slow-wave discharges before treatment.*

B=*tracing sixty days after radioiodine therapy, showing great improvement.*

Three electroencephalograms taken before operation disclosed an irregular slow-wave focus in the right frontal and temporal areas (Fig. 2) while the blood sugar was 38 mg. per 100 cc. Electroencephalograms taken 18, 38, 53, 102, 278 and 286 days after partial pancreatectomy (1 cm. of the tail of the pancreas being removed) showed that this focus persisted even after blood sugar levels had returned to normal, suggesting that hypoglycemia has a more intense effect on some brains than on others, with resulting localized damage that is nonreversible (Fig. 2).

Although there is a general relation between the electroencephalogram and the level of the blood sugar, there are great individual variations. In a given person certain cortical areas may be especially sensitive to generalized hypoglycemia. The duration and the degree of the hypoglycemia are both important determinants of the electroencephalographic response. To get a close relation between the electroencephalogram and the blood sugar level other factors must be taken into account: one must know not only what the blood sugar is but also what it has been previously and for how long. One must also know the differential vulnerability to hypoglycemia of each part of the patient's brain.

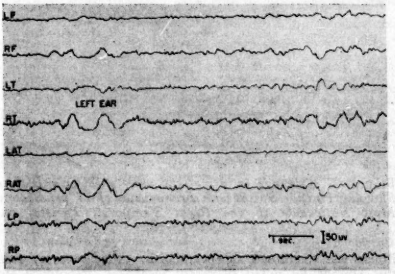

FIGURE 2. *Focal Slowing in the Right Hemisphere, Most Marked in the Temporal, Anterior Temporal and Frontal Areas.*

Addison's Disease

A 37-year-old male high-school teacher was admitted to the hospital with a history of chronic urticaria of 8 years' duration. He had had frequent, severe colds in association with the urticaria. There was also a gradual development of fatigue over 1½ years before admission with weight loss of about 10 pounds. In December, 1951, he became extremely weak and had nausea and vomiting. This episode lasted for 4 days; he was admitted to a private hospital. He went into shock and received blood and fluids intravenously. Recovery was gradual over the next month. At about this time he began to note areas of leukoderma and increased pigmentation. Because of persistent weakness he was admitted to this hospital.

Physical examination revealed an undernourished, chronically ill man who was 6 feet, 1½ inches tall and weighed 116 pounds. There was a generalized increase in pigmentation of the skin, with many dark-brown or black freckles. There were several areas of leukoderma about the elbows and forearms. Examination was otherwise not remarkable.

The blood pressure was 92/80, and the pulse 92.

Blood counts and urinalysis were normal. The nonprotein nitrogen was 46 mg. per 100 cc. The sodium was 130 milliequiv., the potassium 6.9 milliequiv., and the carbon dioxide 21 milliequiv. per liter. The blood sugar was 77 mg. per 100 cc. The total eosinophil count was 377 per cubic millimeter. The urinary 17-ketosteroids was 3 mg., and the 11-oxycorticoids 0.4 mg. per 24 hours.

Eight electroencephalograms were taken while the patient was awake and asleep (Fig. 3). While he was awake high-voltage activity, with a frequency of 9 per second and many runs of slow waves, 6 to 8 per second, were seen, especially in the bifrontal and biparietal areas. During drowsiness and light sleep many positive spikes of 14 per second and occasionally spikes of 6 per second were observed in the right

temporal, parietal and occipital areas, with some involvement of the left. This abnormality persisted for 18 months.

Hypopituitarism

A 38-year-old man was well till 1946, when a febrile illness characterized by high fever, severe, pounding headaches, nausea, vomiting, delirium and loss of consciousness developed. He was admitted to a private hospital, and his

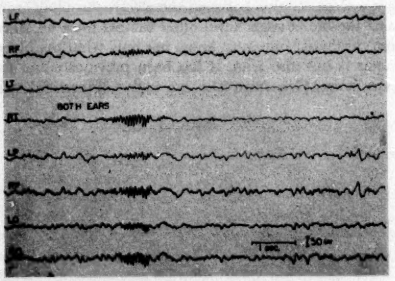

FIGURE 3. *Tracings in a Patient with Addison's Disease, Showing Positive Spikes with Frequencies of 14 per Second, Most Noticeable in the Right Temporal, Parietal and Occipital Areas.*

illness was diagnosed as encephalitis. After recovery from this episode he noted persistent weakness, impotence and the gradual loss of body hair. He was unable to keep a job because of fatigue in ordinary activity.

Physical examination revealed a well developed and well nourished man whose skin was very soft and smooth, with diminution of body hair. There was bilateral testicular atrophy.

The blood pressure was 98/74.

Examination of the blood demonstrated a mild anemia. The basal metabolic rate ranged between +12 and +29

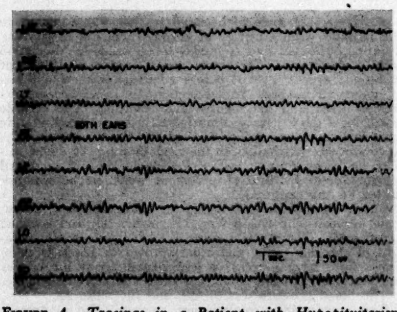

FIGURE 4. *Tracings in a Patient with Hypopituitarism, Showing Positive Spikes with Frequencies of 6 per Second, in the Entire Right Hemisphere.*

per cent. Urinary 17-ketosteroids were 6.4 mg., and 11-oxysteroids 0.78 mg. per 24 hours. An intravenous glucose tolerance test disclosed a flat curve, and an insulin tolerance test caused a hypoglycemic episode. Studies with radioactive iodine were interpreted as normal or low normal. The serum electrolytes showed no remarkable deviations from normal. Skull films and visual fields were normal.

Five electroencephalograms taken while the patient was awake and asleep (Fig. 4) revealed activity of 9 or 10 per second, with generalized, slow waves, 6 to 8 per second, while he was awake. During drowsiness and light sleep there were bursts of positive spike discharges, with frequencies of 14 and 6 per second. There were usually 2 to 4 such discharges in each tracing. The patient was followed for more than 2 years, during which the abnormal pattern persisted.

DISCUSSION

The diagnostic classification and the type of electroencephalographic abnormality in each diagnostic group are shown in Table 1. Forty-two, or 48 per cent, of the patients had abnormal electroencephalographic patterns. Seizure activity occurred in 21 per cent, slow activity in 13 per cent, fast activity in 10 per cent (who had received no sedation for a week before the tracing was taken) and focal slowing suggesting localized damage in 4 cases, or 4 per cent.

TABLE 1. *Electroencephalographic Abnormalities in Various Diseases.*

DIAGNOSIS	PATIENTS WITH NORMAL TRACINGS	PATIENTS WITH POSITIVE SPIKES	PATIENTS WITH SLOW WAVES	PATIENTS WITH FAST WAVES	PATIENTS WITH SLOW WAVES & SPIKES	PATIENTS WITH GENERALIZED SEIZURE DISCHARGES	PATIENTS WITH FOCAL & GENERALIZED SLOWING	PATIENTS WITH FOCAL SLOWING & SPIKES	PATIENTS WITH MIXED FAST & SLOW WAVES
Diabetes	25	2	3	1	2	1	2	1	
Addison's disease	2	2	5			1			
Hyperthyroidism	10	1	2	7	5	1			1
Hypothyroidism	3	1							
Hypoparathyroidism			1						
Hypopituitarism		1							
Pituitary tumor	4						1		
Cushing's disease	1								
Islet-cell adenoma of pancreas							1		

Two of these were patients with diabetes, both of whom had had cerebrovascular accidents. One patient had a pituitary tumor, and the other an islet-cell adenoma of the pancreas.

The frequency of electroencephalographic abnormalities in diabetes is not surprising because the cerebral blood vessels are often involved in persons with severe diabetes. However, the occurrence of seizure discharges in cases of hyperthyroidism, hypopituitarism and Addison's disease is surprising. The commonest type of seizure discharge was the positive spikes at 14 and 6 per second. They are believed to indicate a thalamic or hypothalamic disorder.[13]

Whether in some cases the disorder is primary in the brain or whether in all cases the brain disorder is secondary to the endocrine dysfunction cannot be determined from the present data, but the direction and the nature of the causal linkage between endocrine disease and brain disorder is a subject worthy of

investigation. The work of others, cited above, and our own evaluation of several of the cases in the present series suggest that central-nervous-system disturbances can be produced by endocrine dysfunction. It also seems evident that endocrine dysfunctions can exacerbate or precipitate pre-existing central-nervous-system disorders. The primary defect may be double: one defect may be present in the central nervous system and another in the endocrine system. In any given case the problem is not so much to ascertain whether the central or the endocrine disorder is primary as to assess the role of both and to determine the relation between them. In any case with endocrine disorder, if there is persistent electroencephalographic evidence of seizure activity in spite of endocrine therapy, an effort should be made to treat the epileptic disorder with antiepileptic medication, in the hope of reducing or ameliorating whatever symptoms are present.

Conclusions

Electroencephalographic disorders of types that commonly correlate with epileptic symptomatology are significantly increased in patients with supposedly purely endocrine disorders. This makes it desirable to consider whether or not some symptoms in these cases are primarily or secondarily neuronal rather than purely endocrine.

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USE OF GLYCYRRHIZIN AFTER BILATERAL ADRENALECTOMY*

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IN 1951 Groen et al.[1,2] described the satisfactory maintenance of several patients with Addison's disease by means of glycyrrhizinic acid. Although Addison's disease differs in many respects from the state of complete absence of the adrenal glands, the similarity of the two conditions is striking enough to warrant an evaluation of glycyrrhizinic acid in patients subjected to bilateral adrenalectomy.

Clinical Study

Three patients with metastatic cancer were utilized in this study: a man with papillary carcinoma of the kidney (Case 1), another man with embryonal-cell carcinoma of the right testicle (Case 3) and a woman with adenocarcinoma of the breast (Case 2). The completeness of the adrenalectomies was attested to by repeatedly negative ACTH tests[3] and by the eventual development of adrenal insufficiency in all 3 cases, as well as by autopsy in Case 2.

Ammoniated glycyrrhizin, *U.S.P.* (containing 96 mg. of reducing sugar, 1.9 milliequiv. of sodium and 5.9 milliequiv. of potassium) was introduced into the maintenance regimen one to three months postoperatively, after the minimal dose of cortisone had been well established. Four grams of glycyrrhizin daily was given by mouth in fruit juice in divided doses. The time schedule for the introduction of glycyrrhizin and progressive withdrawal of cortisone is indicated in the charts describing the clinical course, which also present the metabolic and clinical progress of the patients. With the possible exception of Case 1 supplementary sodium chloride was not given at any time in the course of the experiment.

Case Reports

Case 1. E.K. (F.D.H. 485), a 62-year-old retired salesman, had previously been subjected to a nephrectomy on the left for papillary carcinoma of the renal pelvis. Persistent pain in the left costovertebral angle and over the lumbar spine, followed by a loss of 20 pounds in weight, occurred later. On admission to the hospital on March 4, 1952, destruction of the first lumbar vertebra and other evidence of disseminated cancer were found. Subjectively, the patient became progressively weaker.

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On June 19 the left adrenal gland, and on July 10 the right adrenal gland were resected. The daily maintenance dose of cortisone was gradually reduced to 25 mg., and on August 3, 4 gm. of glycyrrhizin was added. During the course of progressive reduction of cortisone and for 8 days on glycyrrhizin alone there were no significant metabolic changes (Fig. 1 and 2). Blood pressure and urinary output were adequately maintained. The patient felt well and was ambulatory. On the 9th day of nonsteroidal maintenance he became slightly lethargic and drowsy; these symptoms became progressively more pronounced throughout the remainder of the study period. On the 10th day of nonsteroidal maintenance, nausea appeared, followed by some vomiting. The resulting poor appetite and fluid intake necessitated supplementary intravenous infusion of 1000 cc. of 5 per cent dextrose in water and 1000 cc. of 5 per cent dextrose in saline solution daily for the remainder of the course.

Concurrent with the development of these symptoms of adrenal insufficiency there was a considerable reduction in urinary output, a fall in serum sodium from 140 to 132 milliequiv. per liter and a drop in blood pressure, both systolic and diastolic (Fig. 1*A* and *B*). There was only a slight rise in serum potassium (Fig. 2*B*) and no change in fasting blood sugar. Although the patient was in obvious adrenal insufficiency, it was decided to increase the dose of glycyrrhizin to 6 gm. daily and to continue to observe him closely. From the 10th to the 22d day of nonsteroidal maintenance his condition grew steadily worse. Although the serum sodium, fasting blood sugar and blood pressure showed only slight variation from their levels on the 10th day, the serum potassium rose sharply, and the urinary output remained scanty. The patient became disoriented on the 22d day, when a severe drop in blood pressure was recorded. Intravenous injection of nor-epinephrine and 100 mg. of cortisone acetate intramuscularly were given immediately. There was a striking clearing of the sensorium. Despite the continued administration of these drugs he failed to respond adequately and died the next day.

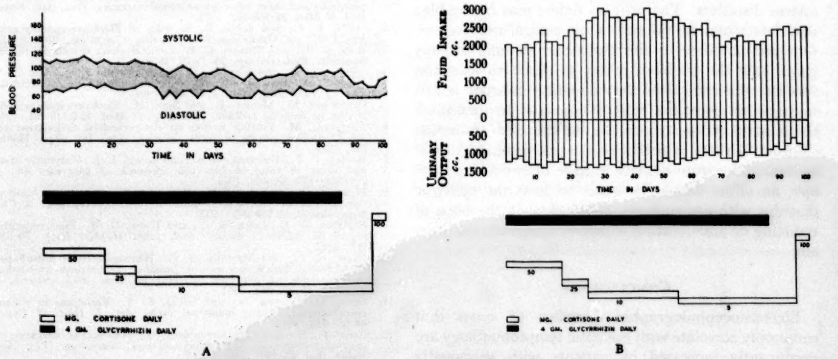

FIGURE 1. *Dosages and Effect of Cortisone and Glycyrrhizin on the Blood Pressure* (A) *and Urinary Output* (B) *in Case 1.*

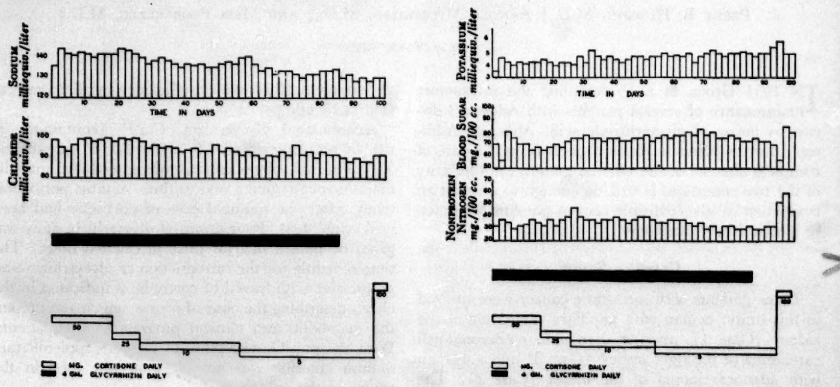

FIGURE 2. *Effect of Cortisone and Glycyrrhizin on the Serum Sodium and Chloride* (A) *and Other Chemical Constituents* (B) *in Case 1.*

CASE 2. R.S. (F.D.H. 1709), a 48-year-old woman, was admitted to the hospital on July 1, 1952, with a diagnosis of metastatic carcinoma of the breast. Radical mastectomy had been performed on the right in 1944, and she had re-

mained asymptomatic until 1950. By 1951 widespread osseous metastasis and progressive paraplegia had developed.

On July 16 a bilateral adrenalectomy was performed. Two weeks after operation the patient was adequately maintained on 25 mg. of cortisone acetate daily. The study period began on August 8, with the addition of 4 gm. of glycyrrhizin to the maintenance regimen.

It was possible to reduce the dose of cortisone gradually to 0 while 4 gm. of glycyrrhizin was administered daily. No appreciable variation in any of the metabolic indexes studied was noted until the daily dosage of cortisone had been reduced to 5 mg. (Fig. 3). Throughout the tapering period the patient, although bed ridden because of osseous metastases, was alert and active. During the 6-day period of 5 mg. of cortisone daily, there was a slight drop in serum sodium and a somewhat greater fall in serum chloride (Fig. 4*A*) and a decline in urinary output (Fig. 3*B*).

On the 24th day of the study cortisone was discontinued completely. For the following 16 days she was subjectively well. However, the serum sodium level exhibited a slow but steady fall. Urinary output continued to decline although fluid intake was good. The variations in serum potassium and blood nonprotein nitrogen followed no consistent pattern, although the fasting blood sugar tended to be low. The 34th day was marked by the onset of drowsiness and lethargy, which persisted and progressively deepened for the remainder of the study. During the next 3 weeks the serum sodium continued to fall slowly, urinary output and fluid intake decreased considerably, the systolic blood pressure was noticeably lower, and the fasting blood sugar declined.

A bout of urinary-tract infection began on the 54th day of the study, and a temperature of 102°F. developed. Cortisone acetate, 100 mg., was given immediately, and the study terminated.

Six months after the end of the experiment the patient died. No residual adrenocortical tissue could be found at autopsy.

Case 3. S.G. (F.D.H. 1734), a 35-year-old congenital mental defective, was transferred to the hospital on July 11, 1952, with a diagnosis of a metastatic embryonal-cell carcinoma of a right undescended testicle. Orchiectomy had been performed on the right at another hospital several months previously.

Physical examination showed an emaciated man, who felt weak and complained of back pain. An abdominal mass was palpable to the right of the umbilicus. X-ray studies confirmed the finding of a mass in the right side of the abdomen. X-ray therapy with the 2,000,000-volt unit resulted in a demonstrable shrinkage of this mass.

Adrenalectomy was performed on the right on September 3 and on the left on October 2. By the end of the 2d postoperative week the patient was adequately maintained on 50 mg. of cortisone acetate daily. The study period began on January 23, 1953, with the addition of 4 gm. of glycyrrhizin to the maintenance regimen.

The cortisone dosage was successfully tapered to 5 mg. daily without any significant alteration of the metabolic functions measured or sense of well-being (Fig. 5 and 6). The patient was active and ambulatory and assisted the ward personnel in minor duties. The reduction in the dosage of cortisone in no way impaired his ability to carry on as before. After several days on the reduced dosage a small, possibly significant drop in serum sodium and chloride occurred (Fig. 6*A*). A slight decrease in urinary output (Fig. 5*B*) and a moderate fall in systolic blood pressure (Fig. 5*A*) were also noted. There was no consistent change in serum potassium, fasting blood sugar or blood nonprotein nitrogen (Fig. 6*B*).

After 1 month on the 5-mg. daily dose of cortisone the 4 gm. of glycyrrhizin was withdrawn from the maintenance schedule. Within 10 days the systolic blood pressure dropped ominously, the urinary output decreased to oliguric levels, and the serum sodium fell to between 129 and 131 milliequiv. per liter. There was a concurrent rise in serum potassium to 5.7 milliequiv. per liter and in the nonprotein nitrogen to 60 mg. per 100 cc. (Fig. 6*B*). During this period the patient became lethargic and drowsy; 100 mg. of cortisone was given at once and for several days thereafter, with good effect.

Some months later an attempt was made to reduce the

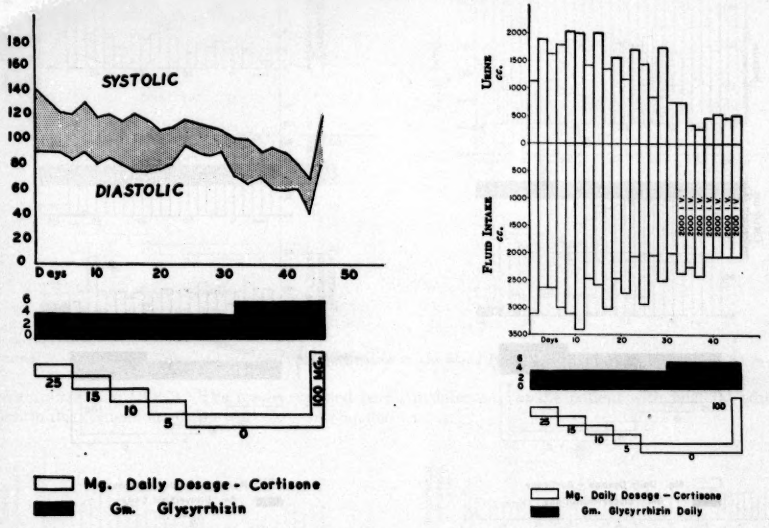

Figure 3. *Dosages and Effect of Cortisone and Glycyrrhizin on the Blood Pressure* (A) *and Urinary Output* (B) *in Case* 2.

dosage of cortisone to 0 with the aid of glycyrrhizin, but it was not possible to do so. However, it was possible to maintain him with 2.5 mg. of cortisone and 4 gm. of glycyrrhizin daily for 3 weeks before the development of acute adrenal insufficiency. The administration of large doses of cortisone promptly restored the adrenal state to normal. He was alive and well 19 months after adrenalectomy.

Discussion

The inadequacy of glycyrrhizinic acid alone for maintaining patients with bilateral adrenalectomy is apparent. However, it is noteworthy that these 3 patients were sustained quite adequately for periods ranging from three to eight weeks upon an amount of cortisone generally considered inadequate.[4] This was achieved by the addition of glycyrrhizinic acid to the maintenance regimen. In 2 cases it was possible to withdraw cortisone completely. Case 1 was maintained for ten days solely on 4 gm. of glycyrrhizinic acid without untoward metabolic changes or any alteration in his sense of well-being. It was also possible to support Case 2 in a similar condition for sixteen days.

In an attempt to evaluate the role of glycyrrhizin in the maintenance of patients on subminimal doses of cortisone, glycyrrhizinic acid was withdrawn from Case 3. Within ten days acute adrenal insufficiency developed. It is conceivable that this occurrence, after the withdrawal of glycyrrhizin, was entirely coincidental. However, the fact that the patient was satisfactorily maintained for one month on a daily dosage of 5 mg. of cortisone and 4 gm. of glycyrrhizin before the withdrawal of glycyrrhizinic acid argues against such a possibility.

The occurrence of drowsiness, lethargy and nausea in Case 1 on the eighth and tenth days of nonsteroidal maintenance was not promptly recognized as clear evidence of impending adrenocortical crisis. From the courses of Cases 2 and 3 it has become apparent that these changes herald the unmistakable syndrome of adrenocortical failure. Nevertheless, it was possible to continue to support these patients, particularly Case 2, for several weeks more with glycyrrhizin alone.

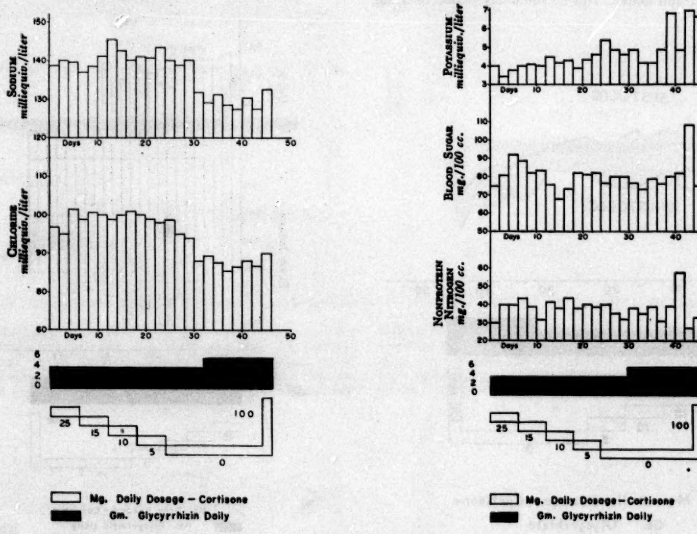

Figure 4. *Effect of Cortisone and Glycyrrhizin on the Serum Sodium and Chloride* (A) *and Other Chemical Constituents* (B) *in Case 2.*

Under the conditions of this experiment the evolution of the syndrome of adrenocortical failure is a gradual one. The levels of serum sodium slowly decline, systolic blood pressure progressively decreases, oliguria develops, and serum potassium rises. This transition occurs over a period of weeks. Throughout the entire study no consistent variation in the level of fasting blood sugar was observed in any of the patients.

In an attempt to elucidate the mechanism whereby glycyrrhizin exerts its adrenocortical-like action, a study of the urinary metabolites of glycyrrhizinic acid was undertaken. The results demonstrate that glycyrrhizinic acid is not metabolized to identifiable steroid substances.[5,6] Groen et al.[1,2] compared the action of glycyrrhizin to that of DOCA (desoxycorticosterone

acetate). They believed that glycyrrhizin contributed more to adequate maintenance of patients with Addi-

Summary and Conclusions

Glycyrrhizin alone is not sufficient for the adequate

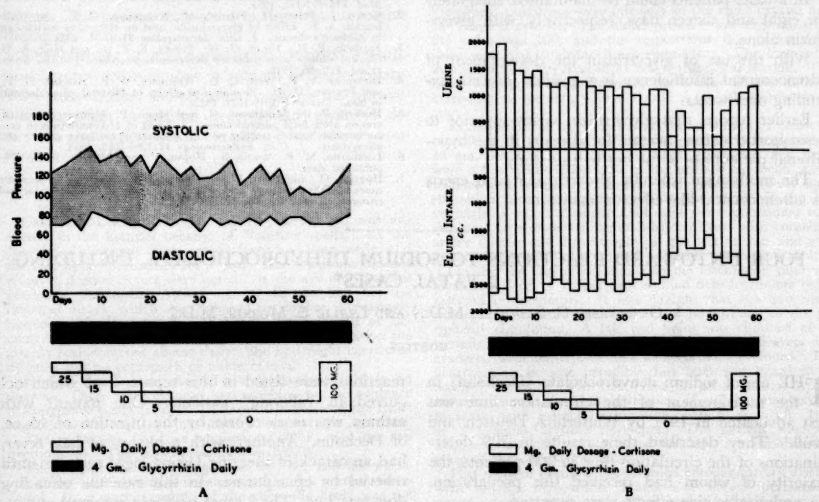

Figure 5. *Dosages and Effect of Cortisone and Glycyrrhizin on the Blood Pressure* (A) *and Urinary Output* (B) *in Case 3.*

son's disease than DOCA. The results reported here confirm this contention. Other workers[4,7] were unable to maintain patients with bilateral adrenalectomy on DOCA exclusively for more than a few days.

maintenance of the patient with bilateral adrenalectomy.

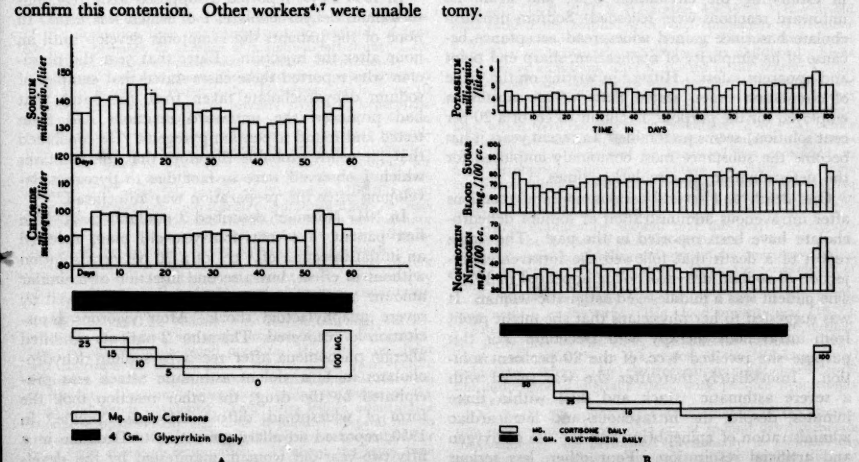

Figure 6. *Effect of Cortisone and Glycyrrhizin on the Serum Sodium and Chloride* (A) *and Other Chemical Constituents* (B) *in Case 3.*

It is possible to maintain patients on heretofore considered subminimal doses of cortisone for periods rang-

ing from three to eight weeks with the addition of glycyrrhizinic acid.

In 2 cases patients could be maintained adequately for eight and sixteen days, respectively, with glycyrrhizin alone.

With the use of glycyrrhizin the development of adrenocortical insufficiency is a gradual process, extending over weeks.

Earlier reports that glycyrrhizin seems superior to desoxycorticosterone acetate for therapy in the hypoadrenal patient are borne out by this study.

The mechanism whereby glycyrrhizinic acid exerts its adrenocortical-like effect is unknown.

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FOUR UNTOWARD REACTIONS TO SODIUM DEHYDROCHOLATE, INCLUDING 2 FATAL CASES*

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BOSTON

THE use of sodium dehydrocholate (Decholin) in the measurement of the circulation time was first advocated in 1931 by Winternitz, Deutsch and Brüll.[1] They described their results in 700 determinations of the circulation time in 300 patients, the majority of whom had received this preparation. No undesirable side effects were reported.

In 1933 Tarr et al.[2] and Gargill[3] also presented favorable reports of their experience with Decholin in estimating the circulation time, and again no untoward reactions were recorded. Sodium dehydrocholate has since gained widespread acceptance because of its simplicity of application, sharp end point and apparent safety. Hitzig,[4] in writing on the value of circulation times, stated that "of all substances employed for the purpose, Decholin (5 cc. of a 20 per cent solution) seems preferable." In recent years it has become the substance most commonly employed for the determination of circulation times.

One death and several serious nonfatal reactions after intravenous administration of sodium dehydrocholate have been reported in the past. The single report of a death that followed the intravenous injection of sodium dehydrocholate appeared in 1936.[5] The patient was a middle-aged asthmatic woman. It was suggested to her physicians that she might profit from intravenous therapy with Decholin. For this purpose she received 4 cc. of the 20 per cent solution. Immediately thereafter she was seized with a severe asthmatic attack and died within three minutes, despite the intravenous and intracardiac administration of epinephrine and the use of oxygen and artificial respiration. Four other, less serious reactions were listed in this report, 2 of which occurred in "allergic" patients. One patient with asthma was made worse by the injection of 15 cc. of Decholin. Another, with a history of hay fever, had an attack of sneezing lasting eight minutes until relieved by epinephrine. In this case the offending dose was 2 cc. The 2 other reactions consisted of nausea and vomiting in patients without a history of allergy.

In 1944 Leys[6] reported 3 supposed toxic reactions to sodium dehydrocholate, 1 of which was fatal. In none of the patients did symptoms develop until an hour after the injection. Later that year the physician who reported these cases stated that samples of sodium dehydrocholate taken from the batch that had produced the untoward reactions had been tested and found to contain pyrogens. He concluded that "it seems probable therefore that the reactions which I observed were in fact due to pyrogens developing after the preparation was autoclaved."

In 1947 Norman[7] described 3 nonfatal cases. The first patient, a seventy-four-year-old man, received an initial injection of 4 cc. of a 20 per cent solution without ill effect, but a second injection of a similar amount administered a week later was followed by severe anaphylactoid shock. After vigorous resuscitation he recovered. The other 2 patients exhibited allergic phenomena after receiving sodium dehydrocholate: in 1, a violent asthmatic attack was precipitated by the drug; the other reaction took the form of widespread, diffuse urticaria. Suckle,[8] in 1950, reported an allergic reaction to Decholin in a fifty-two-year-old woman, manifested by the development of urticaria of the anterior chest wall, marked flushing of the face and pruritus. Three years later Coggins et al.[9] gave a patient 5 cc. of a 20 per cent solution. There was an immediate onset of dyspnea, cyanosis, pallor, profuse sweating and a

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rapid, weak pulse. The blood pressure fell from 220 systolic, 90 diastolic, to 90 systolic, 50 diastolic. The end point for the circulation time was not obtained. The patient responded to vigorous supportive therapy.

The purpose of this paper is to describe 4 additional untoward reactions to sodium dehydrocholate. Two patients died shortly after receiving the intravenous injection of sodium hydrocholate given to determine circulation times; the other 2 had severe, nonfatal reactions.

Case Reports

Case 1 (M.G.H. 157958).* A 15-year-old girl was admitted to the hospital because of "fainting spells." At the age of 5 a diagnosis of rheumatic fever had been made, and she had been hospitalized for 1 year. Her symptoms did not recur, and no murmurs were noted. At the age of 7 cyanosis gradually developed. At the age of 10 she had her 1st syncopal attack, which was followed by similar, increasingly frequent episodes whenever she overexerted herself or became emotionally upset. In the weeks before admission the attacks had occurred almost daily. She had slight exertional dyspnea but no orthopnea or ankle edema.

Physical examination showed a well developed girl in no distress. There were cyanosis and clubbing but no evidence of congestive heart failure. The apical impulse of the heart was felt at the midclavicular line. There were no murmurs.

The pulse was 100, the temperature 99°F., and the respirations 20. The blood pressure was 105/80.

The hemoglobin was 17.7 gm. per 100 cc., and the white-cell count 11,900, with a normal smear and a normal differential. In a roentgenogram of the chest the heart was not enlarged, but the pulmonary artery appeared prominent. In a lateral view the right ventricle seemed to be slightly enlarged. The lungs were clear. An electrocardiogram was consistent with hypertrophy of the right ventricle and sinus arrhythmia.

On the 5th hospital day an arm-to-tongue determination of the circulation time was carried out, to establish, if possible, the presence or absence of a right-to-left shunt; 1 cc. of sodium dehydrocholate was injected intravenously on 2 occasions 1 minute apart. Good end points were obtained at 7 and 8 seconds respectively. However, within 5 to 10 minutes, the patient became severely dyspneic, hyperpneic and more cyanotic than usual, and then restless and soon unresponsive, with a subsequent, brief tonic-clonic convulsion and apnea. She responded to artificial respiration. The blood pressure was 180/120, the pulse 70 (normal for her, 100 to 110), and the respirations 16. She again became apneic. Her pulse fell to 40, to 20 and to 10. Oxygen, artificial respiration, intracardiac administration of epinephrine and direct electric stimulation of the myocardium failed to revive her, and she was pronounced dead 40 minutes after the injection of the sodium dehydrocholate.

At post-mortem examination there was a large defect between the aorta and the pulmonary artery, hypertrophy of the right ventricle and advanced pulmonary endarteritis.

Case 2. (M.G.H. 768439). A 50-year-old man was admitted to the hospital for study because of pulseless extremities and unobtainable blood pressure. His chief complaint was shortness of breath for 1 month. Ten years before admission he had begun to have intermittent claudication of the legs. Two or 3 years later similar symptoms of the arms and hands developed. Two years before admission a lumbar sympathectomy was done at another hospital for an indolent ulcer of the right leg, followed several months later by a right midthigh amputation. At about the same time he began to have infrequent attacks of angina pectoris. Digitalis was started. One month before admission he noticed increasing exertional dyspnea and orthopnea. When seen by a physician he was found to have mild congestive heart failure and pulseless extremities, and the blood pressure was unobtainable. He entered the hospital for study.

Physical examination demonstrated a man who appeared chronically ill, with striking Cheyne–Stokes breathing and variable cyanosis. He had a right midthigh amputation. Peripheral pulsations were felt only in the right carotid and left femoral arteries. The blood pressure was unobtainable; the pulse was 100, and the respirations 0-50. The neck veins were flat, and the lungs were clear. The liver edge was palpable 3 fingerbreadths below the costal margin. The heart was moderately enlarged, the border of the dullness extending to the left, with a Grade 2, apical, systolic murmur.

Examination of the blood disclosed a white-cell count of 13,700, with a normal differential, and a hemoglobin of 13 gm. per 100 cc. There was slight glycosuria, and there were a few white blood cells in the urinary sediment. Electrolytes and nonprotein nitrogen were normal. X-ray films showed a heart enlarged mostly in the region of the left ventricle, a calcified aortic knob and some pulmonary congestion. An electrocardiogram was consistent with coronary-artery disease and hypertrophy of the left atrium and suggested the possibility of an old posterior myocardial infarct.

On the 3rd day after admission the circulation time was measured, 5 cc. of 20 per cent sodium dehydrocholate being injected intravenously. It was thought that this procedure would help to estimate the extent of impairment of the peripheral circulation. A fair end point was obtained at 61 seconds. Ten minutes later severe respiratory distress and cyanosis, with hyperpnea and tachycardia, developed. The heart action became inaudible but later was heard to be forceful, irregular and fast (rate of about 130). Apnea ensued. Intracardiac administration of caffeine and oxygen by mask, with artificial respiration, were of no avail. In 2 or 3 minutes asystole developed. The patient was pronounced dead 20 minutes after the injection for measurement of the circulation time.

Post-mortem examination revealed coronary-artery disease, with an old myocardial infarct and fibrous pericarditis, severe arteriosclerosis, with old thrombosis of the abdominal aorta and marked arteriosclerotic narrowing of most of the major arteries, bilateral hydrothorax, acute pulmonary edema and a recent (about 1 week old) pulmonary infarct.

Case 3 (U. S. P. H. S. H., Boston, 45054).† A 46-year-old man entered the hospital with chief complaints of irregular heart action and dyspnea for 2 days. He had had scarlet fever but no known rheumatic fever in childhood. Eight years before admission, after 3 months in the Marine Corps, he noticed easy fatigability and dyspnea on exertion. He was found to have mitral stenosis and was discharged from the service. He was then well except for episodes of dizziness, which were thought to be functional. Two years before admission he was digitalized because of pulmonary congestion. With this treatment he improved but continued to have orthopnea requiring 2 pillows for relief and some exertional dyspnea. Two days before admission the dyspnea became more severe, and for the 1st time he noted an irregular, rapid heart action.

Physical examination showed that the heart was slightly enlarged, the border of dullness extending to the left, with Grade 2, apical, systolic and presystolic murmurs and a Grade 1, aortic, systolic murmur. There was no evidence of congestive heart failure.

The pulse was grossly irregular, at a rate of 110 at the apex and 76 at the wrist. The blood pressure was 118/72.

The urine, blood and sedimentation rates were normal. An x-ray film of the chest demonstrated cardiac enlargement, predominantly in the region of the left atrium and pulmonary artery. An electrocardiogram disclosed atrial fibrillation and a digitalis effect, with possible hypertrophy of the left ventricle.

On the 2nd hospital day a determination of the circulation time, with injection of 3 cc. of sodium dehydrocholate intravenously, was performed, presumably to establish the presence of congestive heart failure. The patient did not taste the drug but about 5 minutes later complained of feeling weak and frightened. He began to sweat profusely; the pulse and blood pressure were unobtainable, and the heart

*This case was reported in detail as a Massachusetts General Hospital clinicopathological exercise.[9]

†We are indebted to Dr. David S. Citron for permission to present this case, which was from the United States Public Health Service Hospital in Boston.

sounds very distant, with a rate of 30 to 40 a minute. Within 10 minutes, after having the foot of his bed raised and after being given oxygen by mask and caffeine sodium benzoate intravenously, he felt much better, and the blood pressure returned to the previous level, with a pulse that was still rather slow compared to the former rate. An electrocardiogram taken 1 hour after the episode showed atrial fibrillation, with a ventricular rate of 80, and was similar to the one taken previously. Recovery was complete, and the remainder of the hospital course was uneventful.

CASE 4. (B.I.H. M48494). A 69-year-old man was admitted to the hospital for a prostatectomy. He complained of occasional palpitation and of exertional dyspnea of several years' duration. Twenty-six months previously he had suffered a cerebral thrombosis, with a mild residual hemiparesis on the left.

Physical examination revealed a well developed, well nourished man in no discomfort. The pressure was 125/55. The heart was slightly enlarged to the left by palpation and percussion. The rhythm was regular at a rate of 76 per minute. A Grade 3, rough, systolic murmur was heard over the entire precordium and was transmitted to the neck. A few fine, moist rales were present at both lung bases. There was no venous distention; the liver was not palpable, and there was no evidence of peripheral edema. Rectal examination revealed an enlarged, smooth, firm prostate. There was a residual hemiparesis on the left.

Examination of the urine showed ++++ test for albumin, and the sediment contained 2 or 3 white blood cells and 5 to 10 red blood cells per high-power field. Blood studies disclosed a hemoglobin of 15 gm. per 100 cc. and a white count of 8300, with a normal differential. The blood sugar was 104 mg., and the nonprotein nitrogen 36 mg. per 100 cc.

In the course of evaluating the cardiovascular status before surgery a determination of the circulation time with sodium dehydrocholate was performed; 9 cc. of sodium dehydrocholate solution was injected intravenously through a 20-gauge needle in 15 seconds. The patient experienced the characteristic bitter taste 22 seconds later. Three minutes after completion of the test he became acutely dyspneic and tachypneic. He was fully conscious and complained of feeling that "the room was closing in" on him. His face was flushed, and a shaking chill developed. Shortly thereafter he vomited. His pulse was full, rapid and bounding; the blood pressure was 150/100. The temperature rose to 100.8°F. The nail beds appeared cyanotic. Examination of the chest revealed numerous sibilant rhonchi throughout both lung fields. Vomiting continued. Treatment consisted of continuous oxygen by mask, Demerol (75 mg.) and Benadryl (50 mg.) by intramuscular injection and aminophylline (0.5 gm.) by rectal suppository.

The patient's condition improved rapidly, and apart from some coldness of the extremities he appeared to be fully recovered 20 minutes after the onset of the attack. The blood pressure returned to a level of 125/60. An electrocardiogram recorded 30 minutes after the reaction showed a rate of 72 per minute, with occasional unifocal ventricular premature beats, but was otherwise normal. A later electrocardiogram was also normal, without ectopic beats.

DISCUSSION

The pharmacology of bile salts has been studied extensively,[11,12] and it is well known that in heart-lung preparations and in intact laboratory animals these substances can produce bradycardia and hypotension (among other toxic effects). Although it has been suggested that sodium dehydrocholate is the least toxic of these substances,[13] it is the aim of this report to demonstrate that its intravenous administration is not without hazard in man.

In Case 1 a young girl was suffering from marked pulmonary hypertension. Such patients are notoriously likely to die suddenly.[10] From this patient's history it was learned that her "fainting spells" were often precipitated by emotional upsets. The circulation-time measurement may have been extremely disturbing to her and may thus have precipitated syncope, with subsequent death.

Nevertheless, the possible role of sodium dehydrocholate itself in the patient's death also must be considered. Obviously, she had a considerable right-to-left shunt, as evidenced by the cyanosis and clubbing and the autopsy findings. She received 2 cc. of sodium dehydrocholate within a period of one minute. This is a small dose to administer to a normally developed girl of fifteen. Since possibly 50 per cent of the drug entered the systemic circulation without being diluted in the lungs and the left ventricle, there may have been a relation between the injection and the subsequent death. The supposition that this girl was unusually susceptible to the action of sodium dehydrocholate suggests at least a possible contributory mechanism for her sudden death.

In Case 2 hyperpnea and tachycardia followed the injection of sodium dehydrocholate. It is entirely possible that the added stress of this reaction was sufficient to produce further myocardial ischemia and death in a heart that was already compromised by extensive obliterative coronary arteriosclerosis.

Case 3 demonstrates the hypotensive and bradycardic effect of sodium dehydrocholate in an unduly susceptible person.

Case 4 appears to have been a hypersensitivity reaction, although careful questioning failed to uncover any history of allergy.

Our observations and those previously recorded indicate that sodium dehydrocholate may produce gastrointestinal disturbances, cardiac arrhythmias, respiratory embarrassment, hypersensitivity states and, rarely, death. Although the number of reactions is probably quite small the fact remains that sodium dehydrocholate may induce cardiovascular derangements that can be critical in seriously ill patients. Careful selection of patients is undoubtedly of the greatest importance in decreasing the hazard of administering this substance, but even so a certain risk remains. In the 2 fatal cases reported above, the determination of the circulation time promised to be particularly fruitful, and the procedure was done after careful deliberation, with most unfortunate results.

The evidence presented suggests that patients with a history of allergy and those with right-to-left shunts may be particularly vulnerable to the untoward effects of sodium dehydrocholate.

SUMMARY

Determination of the circulation time with intravenous injection of sodium dehydrocholate occasionally produces severe toxic reactions. Four such reactions, 2 of them fatal, are described.

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SPECIAL ARTICLE

BOSTON MEDICAL LIBRARY

Report of the Librarian*

HENRY R. VIETS, M.D.

BOSTON

THE Librarian herewith presents his annual report, the sixteenth accounting of the state of the Library since he took office in 1938. This report covers the calendar year 1953, a year of increased use of the books and journals, with more readers than at any time in the last six years. In addition to the increase in service there was the usual growth of the Library in books and catalogued pamphlets, 378,897 items being made available to readers. It is of interest to notice the trends of the Library since 1936. The increase in size has been between 3000 and 5000 items a year, a normal steady growth for a library of this type. The attendance and circulation have varied, owing to external conditions such as those prevailing in World War II, when, in 1943, only slightly over 6000 persons used the Library and withdrew 25,000 books or pamphlets. Those who used the Library the most were young men and women who in that year were largely in the service. On their return in 1945, the trend moved upward, and it has been relatively steady ever since. There were, in 1953, more than twice as many readers as in 1945, and twice as many items were used; the attendance was 16,061, and the circulation 73,211. This indicates that the men who write the scientific papers, as the result of their laboratory and clinical research, produce in large measure the Progress Reports for the *New England Journal of Medicine* and compile the textbooks and monographs, find the Boston Medical Library an indispensable part of the practice of medicine in the Boston area. The increased use is a sign of healthy growth and indicates a steady rise in the appreciation of valuable collections (Fig. 1). With the opening of the new stacks in the fall of 1954 and the sorting of the accumulated material in the basement, it is expected that the Library will grow at a more rapid rate in future years. This can only mean that increased service will be needed, for it is now becoming apparent that the same number of staff members who served the readers in 1945 can no longer continue to do so when the work load becomes heavier than at present. Even now the staff often finds it difficult to render first-class service to so many readers. Nevertheless, they did so in 1953, greatly to their credit. Not only have they satisfied their clients but also the readers, in turn, have helped by being tolerant in their demands, knowing that the Library is seriously understaffed.

The periodicals currently received remained at slightly over 1000, based on subscriptions, paid and

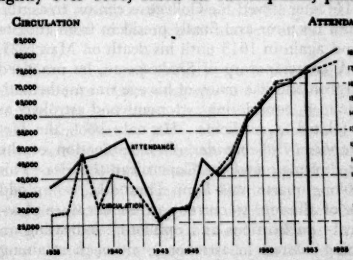

FIGURE 1. *Yearly Attendance and Circulation, 1936-1955.*

free exchanges with the *New England Journal of Medicine* and donations. Slightly over 60 new titles were added, including the following: the *Journal of the American Geriatric Society*, ably edited by the late Willard O. Thompson (who died in March, 1954); *Applied Microbiology*, issued under the sponsorship of the Society of American Bacteriologists; *Obstetrics and Gynecology*, of whose editorial board Arthur T. Hertig is a member; *Najoya Medical Journal* (in English), from the Najoya City University Medical School; the cancer section of *Excerpta Medica*, begun in July, 1953; and *Acta Psychotherapeutica Psychosomatica et*

*Presented at the annual meeting of the Boston Medical Library, May 17, 1954.

Orthopaedagogica, the official organ of the International Society for Special Education (for the care of handicapped persons), with Felix Deutsch as a collaborating editor. The exchange of material of all classes from countries all over the world and the United States showed considerable gain. Relations were entered into with UNESCO in Paris. The Director, while abroad during the summer, attended the First International Congress on Medical Librarianship, held in London, July 20-26, and served as vice-president of the Congress. Subsequently he visited Paris, Rome, Florence, Barcelona and Madrid, greeting old friends of the Library and making new ones. Many books were purchased, greatly to the Library's advantage.

English Imprints Accessions

From funds long held by the Library for the purchase of rare books of medical interest, a number of purchases were made, including some English imprints to add to the small but growing collection of books in this class. The chief additions were as follows: Richard Forster: *Ephemerides Meteorographicae* (London: Joannes Kyngston, 1575); Thomas Coghan: *The Haven of Health* (London: Henrie Midleton, for William Norton, 1584); *The Distiller of London* (London: Richard Bishop, 1639); Daniel Lakin: *A Miraculous Cure of the Prusian Swallow-Knife* (London: J. Okes, 1642); Matthew Mackaile: *Macis Macerata* (Aberdene: John Forbes, 1677).

Astronomy and Astrology. Richard Forster graduated at Oxford, M.B., and M.D. in 1573, and became a fellow of the College of Physicians of London about 1575. He later served the College as censor, treasurer, Lumleian Lecturer and finally president from 1601 to 1604 and again in 1615 until his death on March 27, 1616. A contemporary of Shakespeare, he practiced as a surgeon and like many of his age was mathematically inclined, considering astronomy and astrology as closely related to medicine. His only book, the *Meteorographical Ephemerides*, is a combination of the ancient Ptolemaic and the Copernican theories. This thin, oblong quarto, says Lynn Thorndike, is "an odd mixture of allusions to current astronomical—and astrological—publications and opinions," indicating an awakening interest in astronomy, although retaining the belief of the influence of the heavens on the course of disease.

Bibliographically, the book is of considerable importance. It appears to have been printed in half-sheet imposition—the gatherings D and E print the same text, whereas the new text of signature E is omitted. It is thought by some that this copy is the only book and the only copy that indicates that half-sheet imposition was used in the sixteenth century, but this point needs further study before confirmation. Other copies of Forster's book (*S.T.C.* 11190) are recorded in the British Museum, Oxford University and the Folger Shakespeare Library in Washington.

Scholarly as Forster was, his book does him little credit. His opinion on the surgery of his time would have been more important, for William Clowes, a good judge, speaks of him as "a worthie reader of the surgerie lector in the Phisition's college." To have been made president of the College on two occasions indicates his place of eminence among his professional contemporaries, but his writing falls far short of the standard set by Clowes, Banester, Gerard and the other Elizabethan physicians.

Of meat and drink. Thomas Coghan (Cogan) was a contemporary of Forster. An Oxford M.B. in 1574, he later combined the position of master of the Manchester Grammar School and a practitioner of medicine in the same city. *The Haven of Health* was written, as he indicates in the title, "for the comfort of students" and covers a vast territory of advice on exercise, food, drink, sleep and sane living. Appended is "A short treatise of the plague, and other like contagious diseases, how they may be auoyded" and "Of the sicknesse at Oxforde." The Oxford epidemic, which appears to have been the *Sudor anglicus*, or sweating sickness, lasted from July 1 to August 12, 1577, when 510 men (but no women) died, including 2 judges, "The high shirife, five of the justices, foure counsailours at the lawe, and an atturnie," as well as jurors and others, all while attending court. As symptoms, Cogan mentions the burning fever, great thirst, with the tongue rough and black, gripes, headache, sleeplessness, raving, bleeding from the nose, vomiting and sweating. Death occurred with great rapidity. Within a year or two, a similar pestilence raged all over England.

The Haven of Health was finely printed at London, in 1584, by Henrie Midleton for William Norton. Not a very uncommon book (*S.T.C.* 5478), copies are recorded in the British Museum, Oxford, Cambridge, the Library of Congress and the Huntington, Folger, Armed Forces Medical and Rylands libraries, as well as the Medical Society of London. Another edition (London, 1612) is also in the Boston Medical Library.

Cogan also wrote schoolbooks in Latin, on Cicero, and a devotional book of Biblical sayings. He bequeathed his books to Oriel College at Oxford and left 4d. to each boy in the school at Manchester. Anthony Wood characterized him as "an able Physician and Latinist, a good Neighbour, and an honest Man." Few will quarrel with that estimate; indeed, many a modern physician might hope for so sound a personal tribute.

Rich-spirits, strong-waters, and aquavitae. Under Charles I, the Company of Distillers of London was incorporated by Letters patent in 1638, the seventy-fourth in precedence of the City Guilds. They at once set up a book of rules and directions concerning distillation of strong waters, which was published in 1639. The standards were high; quality was to be rigidly maintained and nothing "meaner, weaker, or any otherwayes inferiour" was to be made, although the distillers were free to make their products "as much

better, richer, or stronger, as you please," but without "tampering" or "pretending to amend."

All vessels were to be properly labeled, so as not to delude the buyer with "false glosses" or "impertinent titles." The rules were printed in a handsome quarto, *The Distiller of London* (London: Richard Bishop, 1639), with the Company's coat of arms, showing a Russian and a Red Indian beside the still. The oath of every free member was appended (*S.T.C.* 16777).

The preliminary notice in the book is furnished by two physicians, Sir Theodore de Mayerne and Sir Thomas Cademan. Their connection with distilling is of some interest, for both were active practitioners of medicine and scholarly men. Mayerne, born near Geneva, graduated M.D. at Montpellier in 1597 and became royal district physician at Paris in 1600. There, he lectured to students, chiefly surgeons and apothecaries, and wrote a treatise on chemical remedies, offensive to the Galenists, which was condemned by the College of Physicians of Paris in 1603. He continued practice, cured an English peer in Paris, who took him to London, where he was warmly received and made physician to the Queen. Oxford granted him an M.D. in 1606 and, after returning to Paris for a time, Mayerne settled in London in 1611, establishing a large and exclusive practice. When James I succeeded Charles, the new king made him his private physician and trusted him implicitly. Mayerne became a fellow of the College of Physicians and wrote the dedication to the first pharmacopoeia published by the college. He maintained a house near Lausanne, in Switzerland, in addition to his London home.

From many of his casebooks, which have been preserved, one learns of his continued interest in chemistry, and he is credited with bringing calomel and the mercurial lotion known as black-wash into use. He experimented in pigments for enamel painting. His notebooks of cases show him to have been a meticulous taker of medical histories and a minute recorder of therapy. He gave a full and lucid account of the typhoid fever of which Prince Henry died in 1612. He was universally respected and always adhered to the principles of medicine in which he was brought up, no trace of courtly servility being found in his writings or ever related of him. Upright in character, he was the great physician of his time. The Distillers of London were indeed fortunate in their founder.

Sir Thomas Cademan, a Cambridge University graduate with an M.D. from Padua in 1620, who held a patent for distilling, was also a fellow of the College of Physicians and a physician to the Queen.

Andrew Grunheide's Abdominal Operation. On May 29, 1635, a young farmer tried to induce vomiting by thrusting a short knife into the back of his throat. The weapon slipped from his fingers and was swallowed, descending into his stomach. On the ninth day "the Rusticke who with an undanted [*sic*] courage waited the Section, was bound to a wooden Table," an incision was made and the knife recovered from the stomach by the "most experienced Chyrurgion and Cutter of the Stone," Master Daniel Schwaben. The abdomen having been opened, the knife was felt in the stomach. This was then extracted by a second cut into the stomach itself, with applause by those standing by and by "the Patient himselfe, who professed that this was the very knife he some daies before had swallowed." The patient made a rapid recovery and was up in ten days. The only anesthetic used appears to have been balsam, given both internally and externally. Five sutures were needed, which were later removed. Grunheide appears to have been operated upon at Königsberg, the nearest university town to his home in East Prussia, after a consultation before the College of Physicians. The original account, written in Latin, was first published in 1636. Dr. Schwaben and his son, Fredericke William, both cutters for stone and cataracts, were lauded by Ladislaus IV, King of Poland, and given certain rights to exclusive territory in his kingdom for the practice of their profession.

Of Daniel Lakin, the translator into English, little is known. He was a much-traveled physician, for notes of his own practice, added to the account of the *Swallow-Knife,* indicate that he operated on a sailor when on a ship in the Gulf of Venice, treated patients in Morocco and was a captive in Constantinople, where he was rescued by the British ambassador, Sir Peter Witch, to whom the book is dedicated.

A Miraculous Cure of the Prusian Swallow-Knife: Being dissected out of his stomach by the Physitians of Regimonto, the chief City in Prusia. Translated out of the Lattin, by Dan. Lakin (London: J. Okes, 1642), contains a woodcut of Grunheide holding up the knife, with the scar of the incision marked on his abdomen (Fig. 2).

Mace, Meat and Drink. Macis Macerata: or, a short treatise, concerning the use of mace, in meat, or drink, and medicine, by Matthew Mackaile (Aberdene, John Forbes, 1677), is an unusual and somewhat rare book. The author, the son of the minister of Trinity College Church, Edinburgh, became an apothecary and burgess of Edinburgh and in his younger days wrote papers on church matters in Scotland. He subsequently practiced medicine in Aberdeen where he received the degree of M.D. from King's College in 1696. His son, who went to Leiden to study physic, became professor of medicine at Marischal College.

In Aberdeen, Matthew Mackaile served as "chirurgian and apothecarie" in 1671, became a "Burger" of the city, fashioned a skeleton, after doing a public dissection, and presented it to the library of Marischal College in 1676, checked a mountebank who had been educated in America, "the most barbarous and ignorant quarters of the world" (1677), "for his impertinently and falsly reflecting upon all the learned physicians" in the city, and wrote, among other things, on mineral springs, cancer and alchemy, as well as his book on mace. He interceded in vain for his cousin,

Hugh Mackail, the covenanter and Scottish martyr, who was hanged at Edinburgh in 1666. During these troublesome times, the pious doctor continued his practice, wrote his books and served as a leading citizen in Aberdeen.

In a seaport such as Aberdeen the importing of nutmeg from the Moluccas was a thriving business. Mace was made from the bark of the nutmeg, an aromatic spice, thought at the time to have medicinal virtues as a simple remedy for stomach and intestinal disorders when added to ale or meat; it is now used as a

FIGURE 2. *Frontispiece from* A miraculous cure of the Prusian swallow-knife. *(London, 1642.)*

condiment or a mild flavoring agent. In an age when an attempt to break the Dutch monopoly in the Moluccas was in progress, Mackaile undoubtedly overemphasized the value of mace to medicine. His small book, however, is a good example of Aberdonian enterprise by a scholarly physician and apothecary. Unfortunately, the Library does not have any of his other works.

Miscellaneous

Maladies des femmes. One of the best historical accounts of the development of midwifery and gynecology is by Irving S. Cutter, in the historical introduction to *Obstetrics and Gynecology*, edited by Arthur H. Curtis, in 3 volumes (Philadelphia and London: W. B. Saunders Company, 1933). Much of the value of the main text of this work has been lost in twenty years, but Cutter's chapter is as fresh as when it was first penned, and the 194 pages, with many illustrations, form a monograph worthy of being bound separately for any historical library. It is not, however, always complete in bibliographic citation.

To Cutter I turn for information about French obstetrics and particularly the part played by Mauriceau, having in mind the first edition of his famous book *Des maladies des femmes grosses et accouchées* (Paris, 1668), acquired by the Library in 1953.

François Mauriceau (1637-1709) was the leading male midwife in Paris in 1668, when he wrote his book. It was based on his vast experience in private practice and at the Hôtel Dieu, the greatest establishment in Europe for lying-in women. The treatise was quickly translated into English (1672) by Hugh Chamberlen, the year before Chamberlen was made physician-in-ordinary to Queen Catherine, wife of Charles II. When Chamberlen was on a visit to Paris in 1670, Mauriceau called him in consultation to see a patient, with a deformed pelvis, that he thought could not be delivered. Chamberlen tried to make the delivery with his forceps (then a secret instrument) for three hours but was defeated, and the patient died the next day. At autopsy the uterus was found torn and perforated in various places. In spite of this disaster, Mauriceau allowed Chamberlen to make the translation of his book, published two years later. The book had a great vogue and soon became the outstanding textbook both in France and in England for all who engaged in the practice of midwifery. At least eight subsequent editions appeared in English, and many in French.

Aphorismes, concerning pregnancy, delivery and diseases of women, was published by Mauriceau in 1694 and later added to *Des maladies des femmes.* The book was designed for midwives and students, containing in succinct form the important material from the larger book. Hunter Robb (*Johns Hopkins Hospital Bulletin* April, 1895) analyzed the aphorisms and found much that was good. Mauriceau, he thought, was an honest, upright man, particularly free from various superstitions prevalent at the time.

Des maladies des femmes is finely printed and illustrated by exquisite copperplate engravings. The Library possesses many other editions of this famous book in French, English, Latin and German. With Mauriceau, the practice of obstetrics may be said to have begun and all that followed in the eighteenth century was a natural corollary.

To the Ramon Lull collection, the Library added *Künstliche eröffnung aller verborgenheyten und geheymnussen der natur, durch woelche die war kunst der Artzney and Alchimey . . .* (Augsburg, 1532), a translation from the Latin version, with a woodcut title page of two men having an animated discussion, presumably about the hidden and secret ways of nature, for the benefit of doctors and alchemists. Lull, a prolific thirteenth-century writer, had many of his works printed in the fifteenth and sixteenth centuries, and some, like this example, were translated into the vernacular. The Library, which has a representative

collection of his works, including three incunabula editions, recently added a complete edition of all his writings in twenty-four volumes, issued 1901-1950 in Palma de Mallorca, where Lull was born about 1236.

The Library also added the Portugese translation of Jenner's *Cow-Pox Inquiry* (Lisbon, 1803) [Le Fanu 42]. It was translated from the second London edition of 1800 and has four finely colored plates.

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MEDICAL PROGRESS

ULCERATIVE COLITIS (Concluded)*

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BOSTON

Carcinoma in Colitis

The possible association of carcinoma of the colon with colitis is of more than academic interest since it may affect the prognosis of a given case and influence the extent of surgical intervention.[93]

Although pathologists, in the past, have denied any relation between the two diseases, more recent studies have emphasized the effect of polyps on the subsequent development of cancer in the ulcerated colon.[94,95]

Of the various types of excrescences that appear attached to the bowel wall, neither the mucosal tags nor inflammatory polyps consisting of mucous membrane and granulation tissue are premalignant.[94] These pseudopolyps, though often considered to be precursors of neoplasm because of their frequent occurrence in colitis, have not been found pathologically to be the seat of any developing carcinoma. Any association between colitis and cancer may be found either in the usual adenomatous polyp, which, though definitely premalignant, is no more numerous in colitis than in normal bowel, or in the mucosal epithelium, in which, under the stimulus of regeneration, foci of precancerous epithelial hyperplasia may develop.[95]

Before the statistical results bearing on this problem are discussed mention should be made of various explanations offered by those who consider this association more apparent than real.[96,97] What seems to be carcinoma secondary to colitis may represent cases of multiple polyposis frequently giving rise to the picture of colitis, which then obscures the underlying polyposis, cases of stenosing carcinoma of the colon, with ulcerations developing proximal to the point of obstruction, or coincidental association of two distinct conditions not etiologically related, especially in elderly patients.

In 1953 the over-all figure for the frequency of carcinoma in colitis was 1.99 per cent out of 4806 patients; the extremes varied from 0 to 6.3 per cent, and the figure included reports from surgical clinics attracting the more seriously involved patients as well as the milder cases seen in private practice or general hospitals.[98] Except for one large series of 855 patients, in which not a single case of carcinoma was found,[99] the consensus of the more recently published statistics is that carcinoma is at least four times more frequent in patients with colitis than in the general population for the same age groups.[100,101] It is also more often found in persons who have had the disease for at least ten years—the longer the duration of colitis, the more likely the development of cancer.[100-104] Clinically, the striking characteristics of the associated lesion are its extreme virulence, the youth of the patients involved and the poor prognosis by the time the diagnosis is recognized and surgery performed.[93,102,103] Moreover, the prevalence is highest among patients who are subjected to surgery, and whose colons are made available for thorough study.[100,103] Finally, ileostomy alone does not protect against the subsequent development of carcinoma, either in the retained colon or even in the rectal stump.[102,104]

Certain suggestions have been offered to explain

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the discrepancies in frequency in different reports.[93,94] Many patients with colitis are not available for follow-up study, and the subsequent malignant degeneration may not be observed by the original reporter. The symptoms of carcinoma may be indistinguishable from those of progressively deteriorating colitis, and the eventual outcome is ascribed to the long-standing colitis, rather than to the more recent, complicating cancer. X-ray and sigmoidoscopic examination may not be adequate to differentiate the diffusely infiltrating intramural carcinoma from the tube-like rigidity of chronic cicatrizing colitis. Thus, among 458 patients who were not operated on, only 9 cases of carcinoma were found by x-ray and sigmoidoscopic study, in contrast to 10 cases found among 226 surgical and autopsied cases. Carcinoma may appear long after the patient has been in a spontaneous remission or even after an ileostomy has led to the impression of a cure so that the carcinoma is considered of independent origin. Biopsies may be unreliable since it is, at times, impossible to distinguish between inflammatory hyperplasia and carcinoma.

It is difficult to explain away such figures as 6.3 per cent of carcinoma among 95 children,[106] a frequency much higher than the calculated expectancy for this age group. It is inconceivable that pathologists of extensive experience would have failed to note (if such information had been forthcoming) that most of these were cases of familial polyposis with ulceration and malignant degeneration rather than primary ulcerative colitis. Moreover, in most, if not all, of these cases, the colitis antedated the appearance of carcinoma by many years. The more recent figures, which reflect the increased frequency of total colectomy, add up to a prevalence of more than 3 per cent for carcinoma in colitis,[93,97,98,102,107] 11 per cent among surgically treated cases[94] and over 20 per cent among those with colitis for over twenty years.[103]

The implications of these figures are especially pertinent to the surgical treatment of colitis. The frequency of malignant degeneration is not sufficiently hazardous to warrant the recommendation of total colectomy for this reason alone.[93] However, once a decision is made for ileostomy because of more cogent additional indications, total colectomy is advisable, since one cannot rely on the usual instructions to the ileostomy patient to remain under constant observation. The patient either feels well and resents the restrictions implicit in frequent examinations or appears for examination only when symptoms become aggravated, thus losing the optimum period for surgery if carcinoma is present. Moreover, the distortion produced by disuse in an inactive colon or rectal stump makes introduction of the sigmoidoscope painful, so that sigmoidoscopic study is as difficult to interpret as to perform.

Associated Disease

In reviewing the associated abnormalities in function and structure one should differentiate those incidental to the toxemia and malnutrition of the primary disease and those specifically related to it. The latter comprise the ileal involvement seen in 10 to 30 per cent of cases of ulcerative colitis, even excluding those with right-sided colitis.[108] Without discussion of any controversy about the relation between ileitis and ulcerative colitis, pathologically it is believed that a distinction can be made between the ileal involvement that represents a spread or backwash from the colon and that primarily involving the ileum. The edematous, hyperplastic and granulomatous appearance of the ileum, with pseudotubercle formation and tendency to fistula formation, in ileitis should serve to distinguish it from the ulcerated and denuded ileum of ulcerative colitis.[108] The recognition of the frequent association of ileal involvement has practical implications in explaining some of the poor results of an ileostomy in which involved ileum was incorporated.

The metabolic changes, with disturbances in electrolyte and mineral balance particularly of calcium, potassium, sodium, and chloride, and dysfunction of steroid secretion reflect the nonspecific sequelae of excessive loss in bloody, purulent exudate, inadequate intake and malabsorption, with resulting malnutrition and even inanition.[56,109,110]

The changes that have been described in the pancreas are primarily those of an interstitial pancreatitis.[111] Other findings are those of moderate fibrosis and, in a few cases, a diminished response to the secretin test.[112] They lend no support to the theory that excessive production of proteolytic enzymes like pancreatic ferments have any striking effect on the production of bowel ulceration. The exact clinical significance of these changes is difficult to assess in relation to the total picture of the patient with colitis. There is no evidence that treatment for these pathologic findings has any bearing on the reversibility of the colitis.

The abnormalities in the kidney are those of endothelial proliferation, with sloughing and obstruction to capillary blood flow only in severely involved cases —11 per cent.[113] It appears that, although the degree of proliferation can be related to the amount of colitis activity, one is not dealing here with any important condition that is readily discernible clinically, such as glomerulonephritis.

Fatty changes in the liver are frequent,[114] without any corresponding increase in the prevalence of cirrhosis.[115,116] Here, again, the findings are not peculiar to colitis but are seen in other conditions accompanied by malnutrition and toxemia with inadequate diet and impaired absorption.[117,118] Disturbances in liver function are common but are usually transitory, varying with the reversible clinical fortunes of ulcerative colitis.

The total picture presented by a study of the associated pathology of colitis enlarges the concept of the disease beyond the narrow confines of the colon to embrace a consideration of many systems. Even though their involvement may be only secondary and of questionable clinical significance at present, the correction

of these abnormalities, whenever possible, may diminish the metabolic burden of the malnourished, chronically sick patient.

Emotions, Psyche and Colitis

Attention has already been called to the various points of similarity between peptic ulcer and ulcerative colitis. This subject is especially relevant in a discussion of the influence of emotions and psyche on the etiology and clinical course of the two diseases.

The modern psychiatric literature on the emotions and colitis began in 1930. In the ensuing ten years almost 60 cases were described in which the impact of psychologic disturbances on physiologic processes was considered etiologically related to the structural organic changes of ulcerative colitis.[119-123] The keynote of this concept of colitis on a psychogenic basis was treatment aimed at the patient's personal problems rather than his bowel symptoms.[124,125]

There is a large body of evidence relating changes in motor, secretory and vascular responses in the colon to stressful life situations.[126,127] With the same technic suggested by a study of gastric physiology patients with colonic fistula were observed directly in response to various stimuli.[128-133] The hyperfunction noted in the bowel was more prominent and sustained in patients with ulcerative colitis, in whom mucosal erosion and superficial ulcerations could be correlated with the emotional states of conflict, hostility and anger. Objectively, increased blood flow, lysozyme production and fragility reflected the somatic reaction of the bowel to disturbing and frustrating aspects in the environment. The proponents of the theory linking stress to colitis considered these functional disturbances as the precursors of structural tissue changes if the inciting stimuli were sufficiently sustained, subsequent bacterial invasion and proteolytic enzymes completing the picture of the pathogenesis of the disease. A further elaboration of this concept visualized the personality structure of the patient as providing an unusually vulnerable target for the disturbing effect of emotional conflict.[128]

A graphic description of the patient with colitis depicts him as being ever anxious to preserve peaceful relations with everyone, even to the extent of making important concessions. This illusion of serenity is often reinforced by a "beatific, angelic look," in contrast to the basic feeling. Similarly, the patients are actually "hostile but appear sweet, anxious but calm, timid but rebellious, with aggressive fantasies but passive behavior."[132]

An extensive study was recently undertaken to determine the relative frequency of certain specific traits in 20 patients with ulcerative colitis.[134] All patients in the group revealed the following: anxiety, tension, inability to assert themselves and sensitivity; with very few exceptions, hostility, guilt, indecision, immaturity, passivity and dependency were found in the rest. Most of these traits and the emotionally immature response to stress existed before the apparent development of the colitis and were not a result of the ravages of the disease, as is often claimed. Although these findings were not limited to the patient with colitis the degree and quality of these traits were combined in him to produce a striking monotony of reactivity to environmental problems. More detailed results of this study in control groups are awaited with interest.

In another report on patients with colitis it was obvious that the personality structure could not be determined on the basis of routine history taking.[135] By means of special technics to elicit significant data all but 1 of these patients were found to be excessively dependent on their parents, outwardly passive and calm, sensitive and fastidious, emotionally immature and beset with excessive maternal dominance. In a control series of 98 unselected patients from the radiotherapy department only 5 resembled those with colitis.

One of the most impressive of all papers on the subject was written by an internist with an obvious orientation in, at least, superficial psychiatric technic.[136] No few words of summary can equal the profit to be derived from a reading of this paper in its entirety. Detailed history taking, rather than the usual routine questioning, showed the personality traits already described by others in addition to hesitating attitude toward ventilating their own characteristics, sham modesty, great need for love and affection, infantile conception of love and reluctance to admit any relation between their emotional conflicts and organic disease. Treatment of these patients, which involved the use of superficial psychotherapy by the internist, consisted primarily of attentiveness, sympathetic care and support, but not psychoanalysis. They were encouraged but never pressed to talk. With improvement in emotional stability they were able to emerge from their dependency relation with their physician, though this could be a traumatic situation in itself, fraught with the danger of recurrence. In 29 patients so treated, 14 remained well for a year after the initial course of treatment, 6 had a recurrence after the initial cure, 7 were improved, and 2 regressed, 1 fatally. These results led to the conclusion that a specific type of emotional conflict was the cause of ulcerative colitis and that the results claimed for other methods of treatment were due to the concomitant support, guidance and care that doctors incidentally gave their patients.

The most common type of environmental problems found to precede the onset of colitis in these studies was the loss of some key figure in the emotional structure of the patient—through death, rejection, removal or disillusionment, to which the patient most often responded with a "grief" reaction.[137] It was rarely advisable to attempt giving intensive insight, explanation or treatment as psychoanalysis, especially during the acute phase of the illness for fear of aggravating the situation. Manipulating the environment or substituting himself in a transference relation for the person lost may represent the physician's chief therapeutic role.

Many of the points of view expressed above have been objected to. At one extreme are those who are convinced, on the basis of their own studies, that colitis has its inception like any infectious disease, without regard to the type of person or the features of his environment.[138] Emotional trauma was only rarely found (1.6 per cent) immediately to precede the onset of colitis and only slightly more often (3.6 per cent) to be associated with recurrences of activity. These reports, in turn, have been criticized as reflecting inadequate technic in eliciting the presence and interpreting the significance of emotional trauma.[139]

The main and middle ground is held by those who maintain that, although the colon may reflect the influence of psychic conflict by functional changes, as seen in the irritable colon, there is no proof that such disturbances can of themselves give rise to inflammation and ulceration characteristic of ulcerative colitis.[14] Secondly, personality characteristics of immaturity and dependency are often seen in the patient with colitis,[140,141] but there is no specific personality profile that can be closely and distinctly correlated with this disease.[123] Studies to the contrary suffer from inadequate controls and lack scientific validity.[142] Psychic trauma, however, often precedes the recurrences and is an important factor in the subsequent clinical course.[143,144] Psychotherapy is an important adjuvant in treatment, especially when limited to a superficial level consisting of support, encouragement and care for the emotional and physical needs. Many patients are too ill to co-operate in any program beyond this. The internist has the best opportunity to supply the dependency needs of the patient without risking aggravation of the tensions and conflicts by too intensive psychotherapeutic involvement. Finally, the natural tendency to spontaneous remissions in over 50 per cent of cases should be borne in mind when one evaluates the specificity of claims made for any therapeutic regimen, including psychotherapy.

Although a few studies have been reported utilizing psychotherapy as the primary and sole method of treatment, it should be considered, for the present, a necessary supplement to a more comprehensive plan of management, combining a constructive patient-physician relation with other generally accepted measures. In an interesting study of patients before and after ileostomy alone, or followed by colectomy, it was possible to separate the basic immature personality development from the superimposed depressive reaction. With remission of the colitis after surgery, the mental depression disappeared, leaving the fundamental personality structure unchanged.[145]

Surgery in Colitis

The treatment of ulcerative colitis is primarily medical. Whereas it may be impossible to pronounce any patient cured, in spite of the length of the remission, if the colon has not been removed,[146] approximately 75 per cent of patients remain in a satisfactory state of health in spite of chronicity and recurrences.[147,148] No more than 10 to 15 per cent require surgery. The indications for surgical intervention are definite in certain cases such as massive hemorrhage, obstruction, carcinoma and perirectal abscesses with rectal stricture, multiple fistulas and anal incontinence.[149,150]

The most commonly cited indication is intractability, and, as in peptic ulcer, this term is difficult to define in any less general terms than failure of medical treatment and chronic social and economic invalidism.[146,148,151] Not only the nature of the treatment prescribed but also the effort made to provide the proper environmental setting for compliance are variants that influence the ultimate designation of intractability and the need for surgery. Some believe that the prevalence of such a status is a reflection of the physician's understanding of his patient and his lack of perseverance in treatment in the face of the discouraging setbacks.[152]

Perforation of the bowel, though seldom leading to free peritonitis, often results fatally, in spite of surgical intervention, which remains the present treatment of choice.[151,153] A few have urged that conservative measures of support and chemotherapy, rather than surgical intervention, may be less hazardous.[154]

Acute fulminating colitis, which constitutes 5 to 10 per cent of all cases, is the most controversial of all indications for surgery. The surgical mortality of emergency ileostomy has been so high (25 to 50 per cent) in these cases that even surgeons have joined with most internists in denying surgery a role in this most dreaded phase of the disease.[149,155] Some of this mortality, undoubtedly, derived from an attitude that referred for ileostomy only moribund patients, as a desperate last measure. Fortunately, the necessity of considering an emergency ileostomy has diminished, with a more optimum time made available for intervention by more recent medical measures. On the other hand a few surgeons have made a plea not only for earlier intervention in the acute toxic cases but also for combining colectomy and ileostomy in one stage.[81,148] The rationale behind this formidable undertaking is that these patients are too sick not to be operated on and that the previous poor results were due to the fact that with ileostomy alone the septic focus in the colon remained a source for increasing toxemia and depletion.[156,157]

Most surgical procedures now combine or follow an ileostomy with a colectomy. The ileostomy in itself is seldom sufficient to produce more than temporary improvement and does not protect the patient from subsequent recurrences and complications, including cancer. The hope of eventually restoring bowel continuity can only rarely be realized, and may lead to malignant degeneration in the rectal

stump retained for this purpose. Only a total removal of the colon will cure the disease, in spite of medical or ileostomy remissions lasting many years.[17,158]

One of the most instructive of all articles on the surgery of ulcerative colitis treats the problem of ileostomy and the considerations involved in making a satisfactory adjustment to it.[151] In addition to the physical indications for surgery it is essential that the patient have sufficient realization of the ravages of the disease to be willing to accept the inconveniences of ileostomy.

The great improvement in surgical statistics, attributable in part to the decrease in emergency ileostomies, chemotherapy and better control of electrolyte, metabolic and nutritional disturbances before and after operation, has been combined with more satisfactory management of ileostomy appliances to present a striking advance in the treatment of ulcerative colitis. In the absence of specific, uniformly successful medical therapy, the challenge offered by surgery has understandably resulted in earlier intervention for patients in whom medical treatment has previously been continued beyond the stage of recovery by any means.[159] It would be most unfortunate, however, if this wave of surgical enthusiasm resulted in too early operation for too many patients.

If only the advice of the fishing guide to his questioning pupil about catching the bass by setting the hook "a split second before the fish is to start on his second run" could be applied with similar effectiveness to the appropriate time for surgery in ulcerative colitis, one would have waited long enough without being too late!

Two additional surgical procedures for the treatment of ulcerative colitis, in an effort to avoid the more radical ones of ileostomy and colectomy, are based on the assumption that interruption of neurogenic pathways supplying the colon will suffice.

Vagotomy

In spite of the fact that fibers of the vagus may not go beyond the distal transverse colon, vagotomy has been described as abolishing spasm and prolonging the colon transit time in ulcerative colitis.[160,161] The rationale of this procedure rests on the finding that diarrhea in dogs after mesenteric ganglionectomy can be prevented by vagotomy. The severe diarrhea that develops soon after vagotomy for peptic ulcer and the general ineffectiveness of anticholinergic drugs in colitis are contrary observations to this concept.[162] The results described are not sufficiently established to warrant general adoption, though good results have been reported in 15 out of 20 cases.[163]

Pelvic Neurectomy

On the assumption that both parasympathetic and sympathetic nerves are excitatory to the colon, an operation has been devised to interrupt the autonomic nerve supply to the pelvic viscera, removing the hypogastric nerves and inferior hypogastric ganglions and part of the sacral parasympathetic network.[164,165] Preliminary results show some improvement in weight gain and a tendency to formed stools, without significant changes in the x-ray appearance of the colon.

Summary and Conclusions

Current contributions to the etiology and pathogenesis of idiopathic ulcerative colitis are briefly reviewed.

Chemotherapeutic agents are not curative but have been of great value in the treatment of septic complications and in preparation for surgery. Their use, however, may be followed by a severe enterocolitis clinically indistinguishable from the disease being treated.

ACTH and cortisone, the most potent drugs available in the treatment of ulcerative colitis, are capable of suppressing abruptly and often dramatically for the duration of their administration, and a variable period thereafter, the clinical manifestations of the acute inflammatory phase, and of influencing favorably appetite, nutrition and sense of well-being. This suppressive effect, which is usually temporary, unpredictable and not always reproducible, limits their usefulness to that of adjuncts in treatment rather than substitutes for more established methods. The possible complications of perforation and bleeding, when added to the usual risks inherent in hormone therapy, militate against their indiscriminate use.

Although this disease has no adverse effect on pregnancy, there is no more serious form of colitis than that first developing during the course of pregnancy. The problems posed by the patient's attitude toward her pregnancy and its effect in possibly creating a stressful family relation may have prognostic significance.

The association of carcinoma of the colon with colitis is assessed in the light of recent statistical surveys, which suggest that the prevalence of carcinoma is greater than that in the general population of the same age group. The long duration and the early age at onset of the colitis favor an increased frequency of malignant degeneration. Ileostomy alone has not offered protection against such a development. The likelihood of cancer is not sufficiently hazardous to serve by itself as an indication for ileostomy and total colectomy. However, when ileostomy is necessary for more imperative reasons, it should be combined with or followed by total colectomy to cure the disease limited to the colon and to remove the threat of carcinoma in this organ.

Theories attributing the structural organic changes in ulcerative colitis to psychologic disturbances are considered. The objections to the etiologic significance of these psychogenic factors, as well as to the specificity of certain personality traits, are discussed. There

is wide agreement about the influence of psychic conflict on functional changes in the colon and the frequency of immaturity and dependency as prominent personality characteristics. Superficial psychotherapy, administered by a sympathetic and interested physician and consisting of support and care for the patient's emotional and physical needs, is an important constituent of any comprehensive plan of treatment.

Although the treatment of ulcerative colitis is primarily medical, total colectomy remains the only method of cure. Improvement in preoperative and postoperative management has resulted in earlier surgical intervention for patients in whom medical treatment had previously been continued beyond the stage of recovery by any means. When surgery has been postponed to the point where it is finally undertaken as a life-saving measure, the optimum period for therapy may have passed.

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MEDICAL INTELLIGENCE

STUDY OF THE USE OF ANTIMICROBIAL AGENTS IN A COMMUNITY HOSPITAL

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NUMEROUS investigators[1-8] have described the development of bacterial resistance after widespread use of various antimicrobial agents. However, concrete reports concerning the extent of their use in different parts of the world are still lacking. An analysis of the use of antimicrobial agents in a 304-bed community hospital in the New England area is herewith presented.

MATERIAL AND RESULTS

The records of all patients discharged from the hospital during September, 1953, were reviewed. The total number of cases was 774, including 143 newborn infants and 173 obstetric cases (143 delivered, 14 abortions and 16 undelivered). Three hundred and twenty-five, or 42 per cent, of the 774 patients had received antimicrobial agents internally during their hospital course. The general medical, dermatologic, cardiac and pediatric cases were grouped as medical

TABLE 1. *Number of Treated Cases and Percentage.*

GROUP	TOTAL NO. OF CASES	NO. OF TREATED CASES	PERCENTAGE OF TOTAL CASES	PERCENTAGE IN TERMS OF 325 TOTAL TREATED CASES
Surgical	623	232	37.3	71.4
Medical	141	88	62.4	27.1
Unclassified	10	5	50.0	1.5
Totals	774	325		100.0

cases. The remaining cases, except 10 unclassified, were grouped as surgical cases; these included all the patients discharged from surgical and obstetric wards and all newborn infants. The number of the treated cases and the percentages in each group are presented in Table 1.

Of the 232 treated surgical cases, 190 patients (81.9 per cent) received the drugs without data available concerning infections at the time of prescription. The drugs were presumably prescribed for prophylaxis or for prevention of dissemination of infections from the infected organs that had been surgically removed, rather than for actual treatment of any existing infections. Two hundred patients (86.2 per cent) among the 232 surgical cases received the drugs as postoperative orders (sometimes after minor surgical procedures such as circumcision and removal of a small tumor). In the 88 medical cases 9 patients (10.2 per cent) received the drugs without data available concerning existing infections at the time of prescription. The total of 325 treated cases was further divided into subgroups according to the number of kinds of drugs used (Table 2).

TABLE 2. *Number of Kinds of Drugs Used.*

DRUG	NO. OF CASES
One kind of antimicrobial agent	185(56.9%)
Two kinds of antimicrobial agents	106(32.6%)
Three or more kinds of antimicrobial agents	34(10.5%)
Total	325

The total dosage and average dosage per patient of each kind of the drugs used are presented in Table 3. A mixture of procaine penicillin G and crystalline potassium penicillin G and streptomycin and a preparation of procaine penicillin G for aqueous injection were most extensively used.

DISCUSSION

Since most of the newborn infants and obstetric patients can be considered as normal subjects, it was expected that the percentage of the treated cases would be low. Of the 143 newborn infants and 173 obstetric patients only 34 received antimicrobial agents. If the cases in these two classifications are excluded, the total number of patients discharged during the month is reduced to 458 and the total number of treated cases to 291, and the percentage of the treated cases is increased to 63.5, which represents a rise of 21.5 per cent in comparison to the 42 per cent given previously. Since the newborn infants and obstetric patients were previously counted as surgical cases, the exclusion of these cases from presentation increases the percentage of treated cases in the surgical group to 64.5, repre-

TABLE 3. *Total Dosage and Average Dosage.*

DRUG	NO. OF PATIENTS	TOTAL DOSAGE USED	AVERAGE DOSE PER PATIENT
Penicillin	312	960,000,000 units	3,100,000 units
Streptomycin	129	764.0 gm.	5.9 gm.
Sulfonamides	48	776.0 gm.	16.2 gm.
Oxytetracycline	17	64.3 gm.	3.8 gm.
Erythromycin	16	51.4 gm.	3.2 gm.
Chlortetracycline	15	49.3 gm.	3.3 gm.
Chloramphenicol	5	25.5 gm.	5.1 gm.

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senting an increase of 27.2 per cent in comparison to 37.3 per cent as given in Table 1.

More surgical than medical patients were discharged from this hospital and, accordingly, the number included more treated cases. However, in terms of percentage the picture is entirely different, because 62.4 per cent of the medical and only 37.3 per cent of the surgical patients discharged were treated. The latter figure can be increased to 64.5 per cent if the newborn infants and the obstetric patients are excluded, as pointed out above.

It is not our intention to evaluate the indications for the use of the antimicrobial agents in individual cases. On the whole, the percentage of the surgical cases treated without data available concerning existing infections at the time of prescription is much higher than the corresponding figure of the medical cases (81.9 per cent in comparison to 10.2 per cent).

This presentation is far from adequate. However, it may serve as a stimulus for further investigation of this problem.

Summary

The use of antimicrobial agents in a 304-bed community hospital during a one-month period in 1953 is reviewed and analyzed.

Forty-two per cent of the patients discharged from the hospital had received one or more antimicrobial agents internally during the hospital course. The figure would be increased to 64 per cent if newborn infants and obstetric patients were excluded.

More surgical than medical patients were treated with the antimicrobial agents; 86.2 per cent of the treated surgical patients received the drugs as postoperative orders. Apparently, more drugs were used for prophylaxis or prevention of dissemination of preexisting infections than for actual treatment.

The number of kinds of drugs used, the total dosage and the average dosage per patient for each kind of drug are analyzed.

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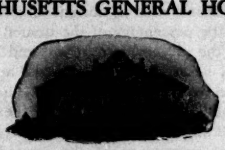
CASE RECORDS
OF THE
MASSACHUSETTS GENERAL HOSPITAL



Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 40411

Presentation of Case

A fifty-eight-year-old woman was admitted to the hospital because of abdominal distress.

Eleven years before admission the patient had had a stroke with left-sided paralysis; however, this gradually improved over a year. For the past year or two she had had episodes of pain in the left anterior side of the chest precipitated by excitement or fatigue and helped a little by nitroglycerin. One and a half years before entry she had had a "heart attack" characterized by severe substernal pain radiating to the left precordium, left shoulder and arm, associated with dyspnea. With this episode she said that she had a "shock," during which she lost consciousness and a complete paralysis of the left side developed. This gradually cleared, leaving minimal residual weakness. She had had a number of identical attacks, three of which occurred in the past three months, for which she had been hospitalized. All these attacks were followed by complete recovery in a few days without apparent disability. However, she felt her heart "grow weaker," with a less forceful beat. The last attack was about three weeks before admission, when she was unconscious for about four hours. When she awoke she still had pain in the chest, arm and back without much shortness of breath. She had had orthopnea requiring 3 pillows for relief for a year, and ankle edema at the end of the day and some puffiness of the hands for six months. Since then she had been taking digitoxin. She said that she had "never weighed more than 150 pounds" until about six months before admission, when she noted gradual weight gain although she had been "eating hardly anything"; two weeks before admission she weighed 220 pounds. About two weeks before admission she started to have constant, unremitting, left-costovertebral-angle pain, spreading to the back and abdomen.

She had had a hysterectomy at thirty-four and a cholecystectomy at forty-five years of age.

Physical examination revealed an agitated, obese woman who, though not appearing to be in pain, complained of severe abdominal pain. The pupils reacted sluggishly to both light and accommodation. Vision in the right eye was decreased. The fundi were not remarkable. The neck veins were not demonstrably distended; the chest was clear to percussion and auscultation. The heart size could not be determined accurately because of obesity. The sounds were distant; the pulmonic second sound was greater than the aortic, and no murmurs, rubs or gallops were heard. There was a regular sinus rhythm. Generalized abdominal tenderness was present but without spasm. There was no edema. Neurologic examination was negative except for weakness of the left arm and leg and marked emotional lability.

The temperature was 98°F., the pulse 80, and the respirations 26. The blood pressure was 120 systolic, 80 diastolic.

The urine was normal. Examination of the blood revealed a hemoglobin of 15.5 gm. per 100 cc. and a white-cell count of 8000, with a normal differential. Stool guaiac tests were negative. An electrocardiogram disclosed a normal sinus rhythm at a rate of 95, a PR interval of 0.18 second, a QRS interval of 0.05 second and prominent P waves and RR′ waves in Leads V_1 and V_2. The T waves were low in Leads 1, 2, aVF and V_6 and inverted in Leads 3, V_1, V_2, V_3, V_4 and V_5. There were occasional premature beats (Fig. 1). A roentgenogram of the chest showed the size of the heart to be at the upper limits of normal. A plain film of the abdomen was normal.

She was transferred to the psychiatric service for study because of persistent agitation without demonstrable organic neurologic disease. On the eighth hospital day, while sitting in a wheel chair, she suddenly became unresponsive, with cold, pale, moist skin, cyanotic lips and fingernails and rapid respiration. The radial pulse and blood pressure were unobtainable; respirations were 30 per minute. The pupils were normal, and the neck veins were slightly distended, though this was difficult to evaluate because of obesity. The chest was clear to percussion and auscultation. The heart sounds were distant with a regular rhythm at 135 per minute. There was a diastolic gallop at the left sternal border in the sixth intercostal space. Approximately twenty minutes after the initial episode she became responsive and complained of severe pain in the chest, both arms and neck. She was given oxygen and 5 mg. of morphine. She vomited once and soon after became unresponsive. Cheyne–Stokes respirations developed, and she became more cyanotic and died.

Differential Diagnosis

Dr. Paul D. White*: I am still continuing my medical education and expect to learn something from this case.

*Member, Board of Consultation (formerly physician), Massachusetts General Hospital.

Before I start the discussion, I should like to ask about the blood Wassermann and Hinton reactions.

Dr. Benjamin Castleman: The blood Hinton test was negative.

Dr. White: In reviewing the electrocardiograms (Fig. 1), I note that the P waves in Leads 2 and 3 are considerably widened and the amplitude is higher than one would expect normally. There are also a few atrial premature beats. In the precordial leads

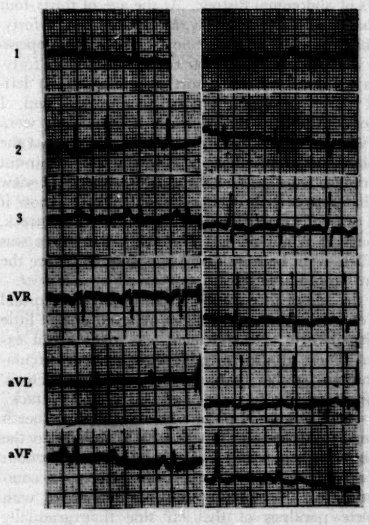


Figure 1.

the T waves are abnormal, being inverted in Leads V_1 through V_5. The R waves are stubby and triphasic in V_1, biphasic in V_2 and prominent in Leads V_3 and V_4. Before I saw this electrocardiogram I thought that the patient's heart was normal, since more than one physician had listened to her heart and none had heard murmurs, and since the remainder of the cardiac examination was negative; now, however, I doubt if the heart was normal. Although the x-ray film showed the heart to be at the upper limits of normal in size, the patient was quite fat and undoubtedly there was fat at the cardiac apex and along its borders.

May I see the x-ray films?

Dr. Joseph Hanelin: The heart is at the upper limits of normal in size, and its configuration is not unusual. The lungs are clear; there is nothing to suggest congestive changes in the lung fields. The abdominal film also appears normal.

Dr. White: Is the left atrium normal?

Dr. Hanelin: I do not see any evidence of enlargement.

DR. WHITE: The pulmonary arc is not prominent. Is it rotated?

DR. HANELIN: Slightly. That would tend to throw its shadow out of the way.

DR. WHITE: This fifty-eight-year-old woman entered the hospital for the last time after about two years of episodes of precordial pain and so-called heart attacks, accompanied by loss of consciousness and temporary left-sided paralysis, and after two weeks of abdominal distress. At the age of thirty-four she had had a hysterectomy, and at the age of forty-five her gall bladder was removed. Both those operations were apparently satisfactory. At the age of forty-seven she had had some sort of stroke with a left-sided paralysis, which gradually improved and, I suppose, cleared in the course of a year. One wonders whether that stroke was like the attacks that she had later on or whether there was a more clear-cut disturbance, such as embolism in the brain. In view of what was described later I should like to know if there was any particular event causing that attack, although it is not necessary to think that there was any such event because nine years went by before the recent symptoms began.

At the age of fifty-six she began to have precordial pain on excitement and fatigue, relieved only a little by nitroglycerin. No statement was made about exertion. These attacks resemble those of neurocirculatory asthenia rather than episodes of angina pectoris. At the age of fifty-seven she had had a "heart attack" with severe substernal pain. One wonders whether it was really substernal. It was said to radiate to the left shoulder and arm. There is no statement about the duration of the substernal pain. Dyspnea accompanied it, and it was followed by another stroke, with complete paralysis of the left side that gradually cleared, leaving minimal weakness. That is not like the attack that occurred when she was thirty-seven years of age; then she apparently had no symptoms connected with the chest. This stroke simulated the other as it went on. She had dyspnea with this attack such as is commonly seen in neurocirculatory asthenia, with hyperventilation and pain.

All these previous attacks had been identical; only 3 occurred in the last three months before she was hospitalized here. The data about the findings at the other hospital are not given. Apparently, there was complete recovery from all those attacks. They do not sound like syncope anginosa although fainting may occur with angina. Nor do they sound like attacks of coronary occlusion or a cerebrovascular accident. Once an attack with an abnormality in the brain—a vascular lesion with paralysis—has occurred in a person with a neurotic constitution subsequent attacks may simulate the first one. Could that attack have been due to hysteria? It was more than neurocirculatory asthenia, or there could have been an exciting factor of pulmonary embolism in some of the episodes.

The edema of the ankles could have been partly due to gross obesity. She apparently gained 70 pounds in less than a year. Could some of the edema have been caused by leg-vein thrombosis at that time?

Then there was costovertebral-angle and back pain for two weeks, for which she entered the hospital. Nothing was found on physical examination; in fact there was only generalized tenderness without any spasm or tumors. Was that true?

DR. ZANVIL A. COHN: That was true.

DR. WHITE: Was there much tenderness?

DR. COHN: Vague tenderness.

DR. WHITE: One wonders whether she could have had more emboli somewhere?

The chief findings on physical examination were the gross obesity and the considerable agitation. She complained of severe abdominal pain but had no spasm. There was no particular abnormality of the heart, lungs or nervous system. The left side of the body was somewhat weak. The neurologic examination and tests were all negative despite the episode of coma and left-sided paralysis. This must be of great diagnostic importance. The neck veins were normal except terminally. There was fever. The blood pressure was normal, but there was a hypertensive background. All the laboratory tests were reported as negative. Was an electroencephalogram done?

DR. COHN: No.

DR. WHITE: Apparently, soon after entry, she was transferred to the psychiatric ward, where I might have sent her, too, on the basis of the history. On the eighth hospital day she suddenly collapsed. The heart rate was 135, and I think there was probably a sinus tachycardia. She woke up in twenty minutes, complaining of chest pain and died soon after that. I do not suppose an electrocardiogram was taken then?

DR. COHN: No; it was not.

DR. WHITE: I believe that she had mitral stenosis despite the negative physical examination—partly because of the possibility of embolism from the heart and partly because of the electrocardiogram—with cerebral embolism on the first occasion, as well as hysteria, neurocirculatory asthenia, gross obesity and terminal, perhaps recurrent, pulmonary embolism.

Before making several diagnoses, hoping that some will be correct and knowing that some, like neurocirculatory asthenia and hysteria, cannot be contradicted, I should like to list other possible conditions. There was no indication that she had a cerebral hemorrhage at the age of forty-seven. She had no hypertension and no local vascular disease. It is not likely that she had an intracranial aneurysm that ruptured, and there was no indication that she had a tumor. There was no history to suggest any of those conditions during the intervening years, and no reason for thrombosis. Embolism, I think, is definitely a possibility.

I do not know for certain whether the sudden onset of hemiplegia may be a hysterical manifestation, but I suspect that it can be. She had not given much evidence of hysteria in the initial attack several years before admission to the hospital. I do not think that she had angina pectoris at fifty-six years of age. I

do not believe that she had coronary atherosclerosis or syphilitic aortitis, which is the background for angina pectoris in the majority of cases. Angina pectoris is seen in mitral stenosis rarely, but I doubt if the symptoms indicated the presence of that in the case under discussion. I think that neurocirculatory asthenia can explain most of the chest pain in a neurotic woman. Acute coronary thrombosis is a possibility, but the attacks were repeated too often; they were all the same, nothing was found afterward, and the electrocardiogram did not resemble that which follows myocardial infarction or coronary thrombosis.

Repeated attacks, with distress and unconsciousness, might have been due to recurrent pulmonary embolism. I suppose such an episode might have been grossly exaggerated by hysteria and neurocirculatory asthenia, but no definite scars or suggestive evidence was noted in the x-ray films. No film of the chest was taken during the final attack, which, I think, was due to pulmonary embolism.

Congestive heart failure is a possibility. I do not think that she had congestive heart failure. Although the heart was slightly enlarged, perhaps as a result of the rheumatic involvement years before, it was not the large heart that is seen with severe congestive heart failure. Breathlessness and edema are not always due to heart failure. As for paroxysmal tachycardia, no note was made that she had a very rapid heart rate at any time until the terminal event. I think that most, if not all, of the fast heart beating was sinus tachycardia.

Intra-abdominal disease should be considered. There was no clear evidence of chronic disease here. The vague pain started in the left costovertebral area, and might have been from the spleen. There was no indication of aneurysm, tumor or vena-cava thrombosis. I do not think that vena-cava thrombosis would have produced that kind of pain although it might have been responsible for pulmonary embolism. There was no indication of any trouble with the endocrine glands. I think that the patient grew fat from overeating, despite the claim that she did not eat much. There is no indication in the electrocardiogram that she had myxedema. There are doubtless other conditions that are either obscure or about which I have not thought.

A PHYSICIAN: Do you think that she could have had a tumor in the right atrium?

DR. WHITE: That would be responsible for what?

A PHYSICIAN: For the repeated attacks of unconsciousness, on the assumption that the tumor acted like a ball-valve thrombus.

DR. WHITE: I think that that is a good suggestion. Such a tumor might have kept the heart from being very large. I had not thought of that possibility.

DR. COHN: There was never much change in the clinical course except during the terminal episode. The pain in the abdomen started in the pit of the stomach and radiated to the left kidney and down the leg.

DR. WHITE: The urine was normal.

DR. COHN: Yes.

DR. WHITE: One thinks of a renal as well as of a splenic embolus. I believe that mitral stenosis, with or without a ball-valve thrombus, is a distinct possibility. Lately, I have known of a number of patients with mitral stenosis who have had no murmurs; the patient under discussion may perhaps fit into that group.

CLINICAL DIAGNOSIS

Acute myocardial infarct.
?Dissecting aneurysm.

DR. PAUL D. WHITE'S DIAGNOSES

Rheumatic heart disease, with mitral stenosis.
Pulmonary embolism.
Cerebral embolism.
Neurocirculatory asthenia.
Hysteria.
Obesity.

ANATOMICAL DIAGNOSES

Fatty heart.
Obesity.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: At autopsy the brain was carefully examined, and nothing was found. We knew the history, so that the neuropathologist made a careful examination of all parts of the brain and found no stigmas of any previous organic disease. It is quite possible that these attacks were hysterical.

The lungs, except for slight congestion, were normal. There was no evidence of embolism or infarction. The heart weighed 570 gm. and was quite striking on gross inspection; the entire epicardial surface was covered with masses of adipose tissue. The fat was so bulky that I asked the prosector to dissect off the epicardial fat. After the epicardial fat had been removed the heart weighed 280 gm.

DR. WHITE: That is about the right ratio for the heart in proportion to the body weight.

DR. CASTLEMAN: Microscopical examination of the wall of the right side of the heart showed only a scattering of myocardial fibers, separated by a great deal of fat (Fig. 2). There was also fatty change on the left side of the heart, but it was not as marked as that in the wall of the right ventricle.

DR. WHITE: How thick was that?

DR. CASTLEMAN: That was about 4 mm., about normal in thickness, but the fibers were quite atrophic. I believe that this is an example of the rare condition of obesity of the heart that sometimes may produce death, perhaps with fibrillation.

DR. WHITE: Was the left ventricle similarly fatty?

DR. CASTLEMAN: It was fatty, but not as strikingly so as the right. I think that if all the fat within the

heart had been extracted the heart probably would have weighed about 200 gm. or less. We found nothing else. The coronary arteries were normal, as Dr. White suspected. There was no organic evidence of any condition that would produce angina. The coronary arteries were almost as smooth as a child's. I notice, Dr. White, that you mentioned this condition in your book.[1]

DR. WHITE: But I do not remember actually having seen a case before.

DR. CASTLEMAN: And you stated that it may be a cause of death. An article in the American literature

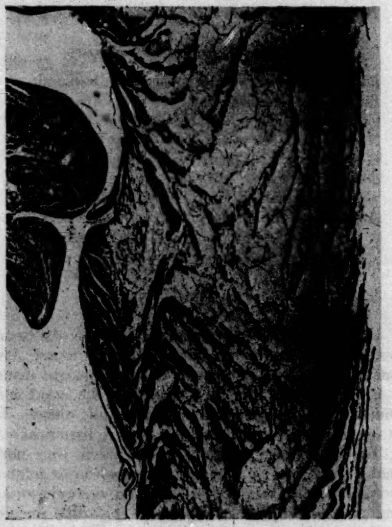


FIGURE 2.

was written in 1933 by Saphir,[2] who reviewed all the reported cases and described 2 similar cases out of a whole group of 50 that showed fatty infiltration without any other cause of death. Those patients died suddenly, as this patient did, although none had had anginal attacks.

DR. WHITE: Did any of Saphir's patients who were obese also have hysterical manifestations?

DR. CASTLEMAN: They were obese, but not with hysterical manifestations. I think that was a separate problem in this case.

DR. WHITE: What was the reason that the patient suddenly began eating so much; was she in a great emotional crisis?

DR. CASTLEMAN: I am not so sure that she was eating so much. I wonder whether there was some other factor that we have not found.

DR. WHITE: There must have been some overeating to produce this fat.

DR. HENRY D. STEBBINS: Was the pituitary gland normal?

DR. CASTLEMAN: On gross examination it was normal. I have not seen the microscopical sections.

DR. ALLEN G. BRAILEY: Have these fatty hearts all been in obese people?

DR. CASTLEMAN: Most of the cases have been in fat people.

DR. BRAILEY: She gained weight very rapidly.

DR. CASTLEMAN: Yes; she said six months—it may have been a year.

DR. WHITE: There must have been another factor; many people who get as fat as that do not have that trouble.

DR. JANET W. MCARTHUR: Was there an islet-cell tumor of the pancreas?

DR. CASTLEMAN: No. A number of cases have been reported—the German literature goes back to 1890 or so—of adiposity of the heart as the cause of death, but whether it was really so I do not know.

DR. WHITE: Formerly, most diagnoses of fatty heart were incorrect, so we have more or less thought that they were all wrongly diagnosed.

DR. CASTLEMAN: This is the first case that we have seen in this hospital in which we could attribute death to a fatty heart.

DR. WHITE: Thank you very much for letting me discuss this case. One more question: Were the atria also involved?

DR. CASTLEMAN: Yes.

DR. WHITE: The T waves over the right ventricle would fit this finding.

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1. White, P. D. *Heart Disease*. Fourth edition. 1015 pp. New York: Macmillan, 1951. Pp. 601 and 602.
2. Saphir, O., and Corrigan, M. Fatty infiltration of myocardium. *Arch. Int. Med.* 52:410-428, 1933.

CASE 40412

PRESENTATION OF CASE

First admission. A twenty-four-year-old woman, gravida II, para II, was admitted to the hospital for study.

Two years before admission the patient began to have slight pain in the lower abdomen, which did not really bother her until eighteen months before entry, when it became so severe that she sought medical aid. At that time she was also having four or five bowel movements daily, rarely with a small amount of blood and with what she described as tenesmus and constipation. Her physician said that her bowels were "overactive." Pills of an unknown nature resulted in only moderate relief. Symptoms continued, however, and she was seen by a number of doctors. The pains were questionably more severe at the time of menstruation, and she decided to have a second child. Symptoms persisted until the seventh month of pregnancy. The baby was born without diffi-

culty about six months before admission. Thereafter, bowel movements were regular, and she had only occasional pain in the left lower quadrant until one month before admission, when, immediately after a menstrual period, she began to have excruciating pain made worse by motion of the left leg or hip. She was more comfortable when she was lying on the left side with the hip flexed. After episodes of pain the abdomen was very tender. She was treated by a gynecologist with some relief, but constipation and straining at stool recurred. She was relatively well until ten days before entry, when pain became severe after the menstrual period and barium-enema examination showed a long, concentric narrowing of the colon, with some shelf formation distally (Fig. 1); therefore, she was referred to the hospital.

Menstrual periods had begun at eleven years of age and had been regular every thirty to thirty-four days. She had had severe dysmenorrhea in the past and had had episodes of constipation for many years. She had lost about 10 pounds during the past several months.

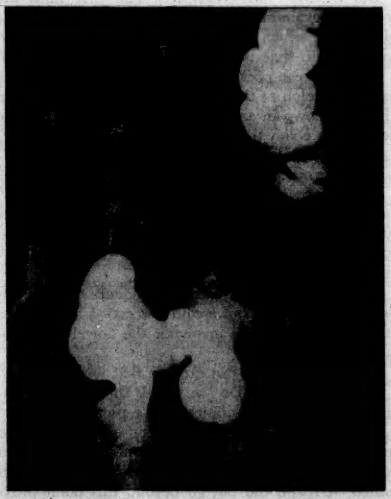


FIGURE 1. *Barium-Enema Examination Before Admission, Showing a Long, Concentric Narrowing of the Colon, with Some Shelf Formation Distally.*

Physical examination revealed a thin, pale woman who complained of pain on moving. The heart and lungs were normal. The left lower quadrant of the abdomen appeared full, and was tender to gentle palpation. There was spasm in the area and a mass that extended to the level of the iliac crest and seemed to extend into the groin. On pelvic examination the vaults were clear; there was pain on movement of the uterus. On rectal examination there was a hard, smooth mass high on the left that was tender and only slightly movable.

The temperature was 99.5°F., the pulse 120, and the respirations 20. The blood pressure was 102 systolic, 60 diastolic.

A urine specimen was normal. Examination of the blood revealed a hemoglobin of 12.2 gm. per 100 cc. and a white-cell count of 19,900, with 80 per cent neutrophils, 16 per cent lymphocytes, 2 per cent monocytes and 2 per cent eosinophils. The serum

FIGURE 2. *Examination Four Days Later on Admission, Showing Extravasation of Contrast Material in Soft Tissue outside the Bowel.*

chloride was 100 milliequiv. per liter, and the total protein 6.5 gm. per 100 cc.

A roentgenogram of the chest was normal. A plain film of the abdomen revealed barium in the descending and sigmoid colon, partially outlining a filling defect in this area. Lying lateral to this was a gas pocket measuring about 5 cm. in length and containing a small amount of barium. There was a considerable amount of gas in many loops of small bowel and considerable fecal material in the ascending colon. Urokon introduced by rectum flowed to the region of the previously described defect, which measured about 10 cm. in length (Fig. 2). There was some lobulation of the distal aspect of the defect. A normal mucosal pattern was not recognized, but true shelf formation was not seen proximally. Contrast substance left the lumen of the colon to fill a large pocket lying laterally and measuring about 10 cm. in length. The colon proximal to the lesion failed to empty.

A gastric tube was passed, antibiotic therapy was begun, and on the fourth hospital day a transverse colostomy was performed. The patient continued to have a low-grade fever and moderate pain and severe tenderness in the left side of the abdomen and groin. Twelve days later a retroperitoneal abscess was drained, with the removal of 240 cc. of fecal-smelling pus. Although there were frequent elevations of the pulse rate to 120, the temperature gradually became normal, and she was discharged with instructions to return later for definitive treatment.

Second admission (one month later). Since discharge she had continued to have a daily temperature of 101°F. and experienced malaise and anorexia. Purulent material had continued to drain from the drainage wound in the left lower quadrant. During the two weeks before admission a mass had developed medial to the previous abscess incision, and during the last few days there had been diffuse swelling in the left groin. Several days before entry a second contrast-medium examination was done. Urokon introduced into the colon flowed to the region of the

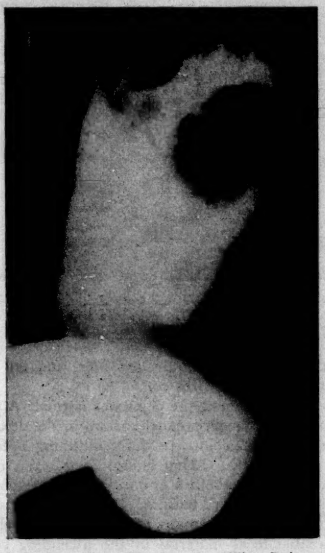


FIGURE 3. *Spot Film, Showing the Filling Defects in the Sigmoid.*

sigmoid and descending colon, at which point the retrograde flow of Urokon was completely obstructed and two rather large intraluminal masses were noted (Fig. 3). There was no evidence of the pocket of gas described on the previous examination. There was still soft-tissue fullness in the left lower part of the abdomen overlying the ilium. The colon emptied well.

On physical examination the findings were as before except for the colostomy, which was functioning well, a hard, mildly tender, fixed mass in the left lower quadrant and the draining sinus. The temperature was 100°F., the pulse 120, and the respirations 20. The blood pressure was 110 systolic, 60 diastolic.

The urine was normal. Examination of the blood revealed a hemoglobin of 12.4 gm. per 100 cc. and a white-cell count of 16,200, with 80 per cent neutrophils, 14 per cent lymphocytes, 2 per cent monocytes, 3 per cent eosinophils and 1 per cent basophils.

The patient was given antibiotic therapy; however, the temperature and pulse remained elevated. On the eighth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. FRANCIS M. INGERSOLL*: Part of this picture is quite clear—that is, the patient had an abscess in the right lower quadrant that involved the bowel and resulted in a perforation, fistula and drainage of this abscess. I am sure that when she first came into the hospital the surgeons had a very clear-cut course of therapy outlined; they defunctioned the bowel in the hope that antibiotics would control the infection. In spite of treatment in the month that followed, the drainage and defunction did not take care of the infection, and for the remainder of the hospitalization the surgeons ran into difficulty in treating this abscess. My problem is to diagnose this process in the left lower quadrant. I think it would be wise to see the x-ray films.

DR. STANLEY M. WYMAN: The first films are from the examination with Urokon made after the plain films, which I shall not show. This area overlying the left iliac wing is filled with Urokon, and is a large abscess pocket that communicates with the narrowed colon at this point (Fig. 2). This spot film (Fig. 3) shows an area of extensive narrowing in the descending colon that corresponds to this area.

DR. INGERSOLL: Where is the lobulation?

DR. WYMAN: This is the lobulation described.

DR. INGERSOLL: Is that due to the fistula?

DR. WYMAN: No; it lies in the distal end of the narrowed portion of the colon. This is the narrowed pathway through the bowel, and one can see no normal mucosa in the area.

DR. INGERSOLL: Is there any evidence of bony disease? Can one rule out a cold abscess—a tuberculous process that might be involving the bowel and producing a fistula?

DR. WYMAN: We can exclude that with certainty.

DR. INGERSOLL: Do you think the skeletal complaints were due to irritation of the psoas muscle?

DR. WYMAN: Yes. In the second examination two very definite, large intraluminal masses are seen in the region where the originally described lobulation existed. Urokon did not go beyond this point proximally. There is no evidence at this time of a gas-containing abscess in this region.

DR. INGERSOLL: They are intraluminal masses?

DR. WYMAN: They are intraluminal filling defects; I cannot define their exact nature, but they are round and irregular.

DR. INGERSOLL: Was it due to fat, or can you say anything about that?

DR. WYMAN: I cannot make any statement about that; I do not think we can differentiate fat from any other type of tissue here.

*Assistant surgeon, Massachusetts General Hospital.

DR. INGERSOLL: They were definitely intraluminal defects rather than defects caused by something bulging into the bowel?

DR. WYMAN: Yes; they were inside the bowel itself.

DR. INGERSOLL: Certain symptoms stand out here that need to be explained. The bowel symptoms seem to have been associated with the menstrual periods. The peculiar fact that the symptoms became so much better during the last two months of pregnancy is hard to explain. Apparently, the perforation of the bowel appeared at the close of a menstrual period, and the patient entered the hospital a month later with an exacerbation of the symptoms also at the close of the menstrual period. I must explain why the drainage of the abscess did not result in rapid improvement of this process. The skeletal trouble I have explained; therefore, I do not need to discuss diseases involving the skeleton.

Being a gynecologist and having been asked to discuss this case, I naturally assume that some gynecologic condition was present; certainly, in the history, the symptoms were all mixed up with menstrual function. I shall list the gynecologic diseases that could result in this bowel condition. Pelvic inflammatory disease can be ruled out by the fact that the patient had a pregnancy in the midst of the disease.

The one gynecologic condition that could give this sort of pattern—and I leaned toward it as a diagnosis before I saw the definite lesion in the x-ray films—is endometriosis. Endometriosis is a lesion that invades tissue; it has been known to invade the sigmoid itself, to cause bleeding and, of course, to have exacerbations and to cause discomfort with menstruation. The pattern that this patient presented makes me think that the ovarian hormones were stimulating some structure that responded and gave her symptoms; therefore, the symptoms occurred at the time of menstruation. We know that endometriosis improves markedly during pregnancy; the fact that the patient's symptoms did improve during the last two months of pregnancy favors endometriosis. Against endometriosis are several obvious features. The patient was only twenty-four years old and had had two children. We usually see endometriosis with infertility and in patients with no children. On the basis of endometriosis I find it impossible to explain the x-ray picture. I can possibly explain the mucosal destruction and even the abscess as caused by rupture of endometriosis, but I cannot account for the intramural masses.

I shall have to turn to the bowel conditions, which, however, do not explain the exacerbation and the difficulty with menstruation. The question of cancer of the sigmoid arises whenever an abscess does not improve after defunction of the bowel and drainage of the abscess. On the other hand the patient had a two-year history and was young; it is difficult to suspect cancer of the bowel at the age of twenty-four. The appearance of the intraluminal lesions makes me consider rare tumors that could account for the symptoms and that do occur in the bowel, such as sarcoma or lymphoma. I have had no previous experience with them so I do not know how rapidly they develop. I should rule them out on the basis of their rarity.

It is possible that she had diverticula. Did you see any in the x-ray films?

DR. WYMAN: We looked for diverticula; there are other films that demonstrated that none were present.

DR. INGERSOLL: Diverticula, too, are incompatible with her age and with her symptoms. The possibility that I must include is that of an unusual infectious process. The one that occurred to me was actinomycosis, so I looked that up and found that it is quite rare in this portion of the colon. Actinomycosis almost always occurs on the right side, involves the appendix and results in fistula on the right rather than on the left side. I suspect that it is possible, but there was nothing to suggest it. Tuberculosis seems unlikely. The possibility that this was some peculiar ulcerative colitis certainly must be considered. This was not the usual picture for ulcerative colitis. I do not know whether ulcerative colitis gets better during pregnancy or whether it is made worse by menstruation. Possibly, this was ulcerative colitis, but although I have not seen many cases, I believe that this was an unusual picture to be related to ulcerative colitis.

Having gone through the list of possibilities and having eliminated all the gynecologic ones, including endometriosis and all the lesions involving the bowel except an unusual bowel tumor such as lymphoma, I shall make that my final diagnosis.

DR. CHARLES G. MIXTER, JR.: Did the patient bleed at any time?

DR. ERNEST M. DALAND: Yes.

DR. INGERSOLL: She had bled with the diarrhea eighteen months before entry.

DR. DANIEL S. ELLIS: As I read over the history I wondered whether she had ulcerative colitis, with which a neoplasm had developed, though that is not as likely as the diagnosis that Dr. Ingersoll made.

DR. BENJAMIN CASTLEMAN: Dr. Daland, will you tell us your opinion before operation?

DR. DALAND: I had one other film, which had been taken five days before entry and showed the same long, narrow constriction. Dr. Wyman added to the difficulty of diagnosis by giving Urokon and demonstrating an abscess cavity; before that we had considered endometriosis, lymphoma and carcinoma. I recall that a graduate nurse standing beside me said that the fact that the patient was twenty-four and had had two children ruled out endometriosis; I was inclined to believe that the nurse was right. After the x-ray picture we were certain that she had an abscess and therefore decided to defunction the bowel with a transverse colostomy. Our previous films had shown that the transverse colon was very low so we did a transverse colostomy by a right muscle-splitting incision. At that time I explored the liver, which was normal. We

purposely did not explore the mass in the left lower quadrant because we believed it was due to a perforation from a bowel lesion and we have learned to keep our hands away from those lesions until we are ready to remove them. We did find one lymph node in the omentum that we removed; it was reported as showing chronic inflammation.

The patient did not improve much after the defunctioning. When she came back to the hospital it was evident that the abscess had to be drained, so it was drained extraperitoneally and a large amount of pus was obtained. The sensitivity tests showed that chloramphenicol was the only effective drug, and it was given to her without improvement—she continued to drain pus and to run a high temperature. The later x-ray films disclosed a mass within the lumen and we thought that she had a neoplasm after all. We were then faced with this dilemma: colostomy on one side and the draining abscess on the other. We went in between the two incisions to explore the abdomen and found a definite tumor involving the sigmoid but did not explore the abdomen further. With one hand in the abdominal incision and a finger in the abscess cavity, the finger entered the bowel and palpated the tumor. A biopsy specimen was scraped off with the finger. The wound remained clean in spite of this maneuver.

Clinical Diagnosis

?Neoplasm of sigmoid.

Dr. Francis M. Ingersoll's Diagnosis

Malignant lymphoma of sigmoid.

Anatomical Diagnosis

Adenocarcinoma, Grade 2, of sigmoid.

Pathological Discussion

Dr. Castleman: The biopsy that Dr. Daland removed showed a characteristic adenocarcinoma of the bowel (Fig. 4). Since we did not have any adjacent bowel we could not say whether there was an underlying ulcerative colitis. Of course, there does not need to be a pre-existing ulcerative colitis; we have seen adenocarcinoma of the bowel in young people.

Dr. Ellis: We can usually see ulcerative colitis distal to the lesion in the sigmoidoscope. Was such an examination done?

Dr. Daland: Yes; it was negative.

Dr. Castleman: The diagnosis was made about six weeks ago. How is the patient now, Dr. Daland?

Dr. Daland: We were then puzzled about what to do. We thought this was an operable lesion, except for the extensive infection; we knew that any attempt at resection would give her generalized peritonitis. We discussed it with the radiologists, who said that there was very little chance that x-ray treatment would do her any good but they were willing to try.

One week after the exploration and biopsy she was treated with the 2,000,000-volt x-ray unit at the daily rate of 300 r (air dose). After eighteen treatments had been given there was a rest period of two weeks. Over a seven-week period she received 5500 r to the tumor. She tolerated the treatment well and had no gastrointestinal symptoms.

Figure 4.

Addendum

Dr. Daland: Five weeks after the x-ray treatments had been completed an exploratory laparotomy was performed. There were no adhesions within the abdomen. There was no fluid and no sign of peritoneal spread. The mass had shrunk to 4 cm. in length and was firmly adherent to the abscess sinus. It was possible to resect the bowel and the lateral peritoneum and also the sinus tract through which the previous biopsy had been taken.

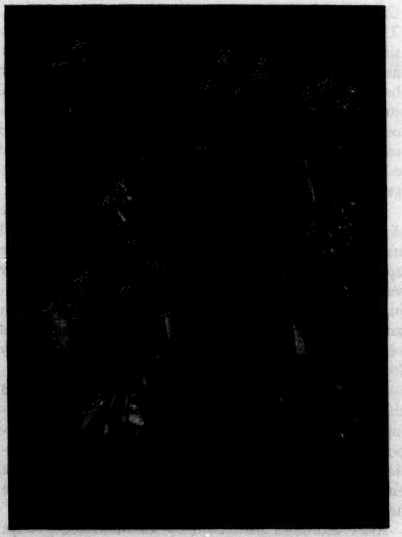
Dr. Castleman: The specimen of sigmoid was about 10 cm. in length and was constricted in its center over an area 3 or 4 mm. in length, the point of constriction admitting only a 1-mm. probe. On each side of the constriction the bowel expanded rapidly to a circumference of 6.5 cm. Although the bowel wall and pericolic fat were thickened in the region of the stricture, there was no gross evidence of tumor either inside or outside the bowel. There was a defect in the bowel just to one side of the stricture that led into the sinus tract, but here also no tumor was seen. Startling as it may seem, microscopical examination of the entire specimen, by quasi-serial sectioning, revealed no trace of carcinoma.

The diagnosis of carcinoma was originally made in February, 1953, and I postponed publishing this case because I could not believe that this well differentiated adenocarcinoma had really disappeared under the x-ray treatment. There has now been a follow-up period of over a year and a half, during which the patient has had the transverse colostomy closed, and as far as can be determined by physical and x-ray examinations is entirely well.

Although I cannot prove that the x-ray treatment did not destroy the cancer completely, I should prefer to reconstruct the sequence as follows: the tumor may have been polypoid in nature and may have intermittently intussuscepted during the two-year period before admission (this is quite consistent with the history), and, as so often happens, the wall of the bowel may have become infarcted with the development of the pericolic abscess. At operation Dr. Daland was able to get a biopsy of the tumor when his finger entered the bowel and either his manipulation or the later radiation broke an already necrotic stalk so that it allowed the polyp to slough.

This case is not unlike the one recently reported from the Mayo Clinic with the unusual title of "Disappearance, probably Spontaneous, of Locally Inoperable Carcinoma of the Descending Colon."* The authors state: "It seems most unlikely that it [the disappearance of the carcinoma] resulted solely from roentgen therapy. The less anaplastic adenocarcinomas of the colon are relatively radioresistant." In their case the colon segment and its mesocolon disappeared and they believed it was due to infarction and ultimate absorption. They ended their report with this pertinent statement: "This case, while obviously most unusual, serves well to emphasize the uncertainties inherent in prognosis, particularly after treatment of malignant lesions. The not infrequent, marked variations from the usual pattern of biologic behavior of malignant lesions should not be forgotten when ultimate outcome in an individual is being considered."

*Fergeson, J. O., and Black, B. M. Disappearance, probably spontaneous, of locally inoperable carcinoma of descending colon: report of case. *Proc. Staff Meet., Mayo Clin.* 29:407-410, 1954.



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30. Lady with Parasol

Hammered Copper by

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Medical Staff, Massachusetts Women's Hospital

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THE HARVEY CUSHING SOCIETY

IN this issue is published the scholarly presidential address of Dr. Edgar A. Kahn, the head of the Harvey Cushing Society in 1954. Because the Society reached its maturity in 1953 and because it is today the largest organization of neurologic surgeons in the world, as well as because of the increasing integration of neurologic surgery with other specialties and with general surgery, it is appropriate at this time to review briefly its origin and development. These have been well summarized in a previous presidential address by Dr. William J. German.*

Until 1920, neurosurgeons were highly individualized, the specialty was in its infancy, and no attempt at organization had been made. In March of that year, however, 11 men who either specialized in or had a special interest in and facilities for doing neurologic surgery met at the Peter Bent Brigham Hospital in Boston and organized themselves into The Society of Neurological Surgeons. From this beginning arose either directly or indirectly all subsequent neurosurgical organizations, including the Harvey Cushing Society.

This latter was organized in its turn in the auditorium of the Children's Hospital (now the Children's Medical Center) in Boston, in May, 1932. After a few years of settling down and a selective influx of new members, the Society, in 1943 or thereabouts, sponsored the publication by Charles C Thomas of the *Journal of Neurosurgery*, with the distinguished neuropathologist, Dr. Louise Eisenhardt, as managing editor. The ever-growing subscription list to this magazine as well as the astute editorial judgment of its managing editor soon not only demonstrated that it was filling a literary niche that had remained empty too long but also gave evidence of a tremendous increase in the numbers of neurosurgeons then practicing in this country.

This fact was substantiated by the experience of the American Board of Neurosurgery, officially activated in 1940 after having been launched in 1938 with the approval of the Harvey Cushing Society. The latter venture was also a success, and the standards of training and other basic requirements promulgated then and later have brought order out of the earlier chaos of resident training, together with increasing safety for the long-suffering public.

Such standardization of training, in turn, showed the necessity of making available to this ever-increasing group of well regulated neurosurgeons some opportunity for the interchange of ideas, the presentation of new methods, concepts and technics and the encouragement of effective productivity among the neophytes in the field.

After thorough discussion by all interested groups it was decided to make the Harvey Cushing Society the largest and most accessible and to keep the So-

*German, W. J. Neurological surgery: its past, present and future. *J. Neurosurg.* 10:526-538, 1953.

ciety of Neurological Surgeons the smallest and least accessible neurosurgical organization. Accordingly, the standards of admission to membership in the Harvey Cushing Society were changed so that any neurosurgeon certified by the Neurosurgical Board, proposed and sponsored by two active members of the Society and approved by the Society's executive committee, could be virtually certain of election by the membership at large. Already the wisdom of this move is apparent, and the influence of the Society for good is testified to by the list of eminent gentlemen who have been honored by its presidency.

The last to be so honored and the author of the paper published herewith is the distinguished successor of his no less distinguished preceptor at the University of Michigan Medical School in Ann Arbor, Michigan. His subject matter shows the catholicity of present-day neurosurgery, and his scholarly and restrained handling of his material and conclusions evidence the necessary universal surgical and medical knowledge now mandatory for any surgical specialist.

This but emphasizes the wisdom of the founders of organized neurosurgery in this country as well as the intelligence and breadth of view of the men to whom they delegated their aspirations, ideals, rectitude and determination that the welfare of the patient must ever have first and foremost consideration.

CARE OF THE PATIENT

References to the care of the patient have become so much a routine matter in any discussion of medical science, practice or economics that there is a tendency to overlook the real significance of the term. Overfamiliarity with the expression may lead to a loss of contact with its meaning and of respect for its importance as the reason for the existence of everything pertaining to medicine and medical science; to doctors, to nurses and to hospitals.

It was in order that this importance should not be lost that the National Commission on the Care of the Patient was initiated by the American Hospital Association in 1948. The Commission, which included representatives from the American Medical Association, the American Hospital Association, the American Nurses Association and the National League for Nursing, suggested the establishment of similar committees at state level, and accordingly a joint committee on improvement of patient care was established by the Massachusetts Medical Society in 1953 with representation from the Massachusetts Hospital and the Massachusetts Nurses associations. An informal preliminary report has been prepared by Dr. Maurice Fremont-Smith, chairman of the committee, and appears elsewhere in this issue of the *Journal*.

As a result of the five meetings held by this committee so far, in which discussion was apparently both frank and free, certain inferences may be drawn. Nursing service having been the main topic of these early discussions it became apparent that the potentialities of the nurse have not been generally utilized to their best advantage, a fault for which the physician must take a large part of the blame. The physician, apparently, has failed more than any other of the human elements involved to join the patient-care lineup as a co-operating factor. Best fitted to lead the team he neither leads nor participates in its joint effort, performing too independently his own functions in regard to patient care.

The Committee, in fact, has astutely put its collective finger on man's greatest failing in the matter of mutual enterprise and human relations — namely, lack of communication. Bitter words and futile quarrels are the result almost always of failures in sober communication at the state where ideas need most to be interchanged. Beginning with communication some such alliterative formula might be produced as:

communication + co-operation + committee = co-ordination − constraint.

In general, "essential" hospital care has been defined as safety, comfort and nutrition, with regular meals (for those who can eat) taking precedence over the other hospital services. The aphorism that a man's heart is best reached through his stomach is a rule that even the cardiologists may follow.

To implement its ideas the Committee has invited 12 Massachusetts hospitals to form trial interdepartmental committees.

PROLONGED-ILLNESS CERTIFICATE

It has recently become increasingly apparent that Blue Cross and Blue Shield plans cannot meet the legitimate requirements of the public with programs that cover only the acute phases of illness and injury. For this reason the prolonged-illness certificate recently placed on the market by Blue Cross and Blue Shield in Massachusetts comes as a welcome extension of their basic coverage.

Unlike the so-called catastrophic or major medical contracts written by insurance companies, which usually require the patient to pay a substantial sum out of his own pocket before the insurance takes over, Blue Cross and Blue Shield have designated 18 conditions that are covered both in and out of the hospital under a continuous and uninterrupted extension of their basic benefits. To classify these conditions the total case load of the Visiting Nurse Association of Boston was examined, nursing-home representatives were consulted, and the two major classifications of illness and injury were scrutinized. The only chronic conditions omitted intentionally are diabetes and arthritis. After definitive treatment or evaluation in the hospital the medical expenses connected with diabetes are looked upon as being budgetable rather than insurable. It is admitted frankly that certain cases of arthritis should be covered but so far a satisfactory line of demarcation has not been agreed upon.

The fact that pre-existing conditions are excluded permanently from coverage is understandable when it is realized that the potential total liability of Blue Cross and Blue Shield in each case is $5,000. Perhaps as experience is accumulated this limitation can be modified to some extent.

One of the most important features of the proposal is its cost—$1 per month per individual subscriber and $2 per month per family. Of these amounts only a quarter is allocated for payments to physicians. Translated into annual subscription charges this means that basic Blue Shield Plan B coverage with the Blue Shield portion of prolonged-illness coverage costs the family only $63 per year. Compared to the subscription charges made by plans that provide so-called comprehensive coverage of physicians' services through group practice this amount is surprisingly small.

It is understood that Blue Cross and Blue Shield are currently working on a low-cost diagnostic-services certificate, which will fill the one major remaining gap in their program. When this work is completed the people of Massachusetts will have available virtually complete protection against medical and hospital expenses of economic significance.

The subscribers, hospitals and physicians who have made Blue Cross and Blue Shield in Massachusetts two of the outstanding plans in the country are to be congratulated.

AMERICAN MEDICAL HISTORY IN 1953

One of the most useful functions of the American Association of the History of Medicine is the publication each year in its bulletin of a bibliography of the history of medicine of the United States and Canada. For the last six years the bibliography has been expertly edited by Professor Whitfield J. Bell, Jr., formerly of Dickinson College in Carlisle, Pennsylvania, and now the assistant editor, under the auspices of the American Philosophical Society and Yale University, of the *Papers of Benjamin Franklin*. Medicine rarely has found a more devoted lay friend than Professor Bell, who has set a bibliographic standard duplicated by but a few of the medical profession. Because he has resigned after completing his sixth bibliography, for the year 1953, it is welcome news that Miss Genevieve Miller, of Cleveland, will succeed him as editor. Bell, like Richard H. Shryock, Lynn Thorndike, George Sarton, Max H. Fisch and Dorothy M. Schullian, Martha Gnudi, Janet Doe and others, has reinforced and augmented the work of Arnold C. Klebs, Harvey Cushing, John F. Fulton, Sanford V. Larkey, Claudius F. Mayer, Sir William Osler, W. W. Francis and Geoffrey Keynes. The scholarly booksellers, Ernst Weil, the late E. P. Goldschmidt, Wilfred M. Voynich, A. S. W. Rosenbach, and many of their colleagues have also had their impact on medical bibliography, although not so directly on the evaluation of American medical literature as the librarians, such as J. C. Bay, J. F. Ballard, J. S. Billings and Archibald Malloch. The stimulus in the twentieth century has come from many sources, and medicine has been enriched in the process.

This rousing influence is reflected in the growth of interest in the history of medicine in both the United States and Canada. Bell records over 100 biographic books or papers on American or Canadian physicians in 1953, ranging from Robert Abbe to Hugh H. Young. Many names are familiar, such as Banting, Beaumont, Cullen, Drake, Grenfell, Halsted, Holmes, Kane, Lahey, Malloch, Osler, Reed, Sims, John Warren and Welch, but a re-evaluation of their work has frequently thrown new light on their personality and the influence they exerted in their time and subsequently. Lesser names also appear, some, but not all, for the first time: William A. Caruthers, the chronicler of the cavaliers; Jonathan Knight and his library; Cornelius W. Larison, exponent of phonetic spelling; Samuel B. Morrison, Stonewall Jackson's physician; Richard Pindell and his one-man army; Eli Todd, of the Hartford Retreat; and Ernst M. Adam, through his unpublished autobiography. The history of at least 10 diseases is referred to in other papers, and there are numerous contributions on medical journalism, libraries, museums, education, nursing, pharmacy, Indian medicine and professional history.

A study of the publications on local history discloses the trend of activity in various parts of the country. The most productive state was Minnesota, with 17 books or papers. Texas followed closely with 13, New Jersey with 10, and Ohio with 9. The other states were all under 6. Massachusetts contributed only 2, as did Connecticut. Illinois was in a class with Georgia, Maine, Maryland, Rhode Island, South Dakota, Alabama, Arizona and Virginia, with only 1 each. Thus, Minnesota in the North and Texas in the South, as far as published papers in 1953 were concerned, lead the field in historical research. The North-West was silent, and much of the Middle-West. One cannot but hope that the tempo set by Minnesota and Texas will spread westward in the near future, New England and most of the East Coast being already quite thoroughly documented. The history of American and Canadian medicine, when it comes to be written, will find a rich store of new material in the annual bibliographies so completely produced by the American Association of the History of Medicine.

Dr. W. R. Wilde, author of a life of Swift, a clever work on the Boyne and Blackwater, and other productions, has been made surgeon-oculist to the Queen, in Dublin, out of respect for his literary merits.

Boston M. & S. J., *Oct. 18, 1854*

MASSACHUSETTS MEDICAL SOCIETY

JOINT COMMITTEE ON IMPROVEMENT OF PATIENT CARE

The following informal report of the Joint Committee on Improvement of Patient Care has been submitted for publication by the chairman, Dr. Maurice Fremont-Smith:

This Committee has been struggling during the past year with a number of debatable and momentarily unanswerable problems. It is felt that these problems should be presented for wider consideration by the profession. They concern the very reason for the existence of doctors: i.e. the better care of the patient.

In 1948, initiated by the American Hospital Association, a National Commission on the Care of the Patient was formed. This Commission included representatives from the American Medical Association, American Hospital Association, American Nurses Association and the National League for Nursing. Discussion embraced chiefly nursing problems; nursing shortages, the education of nurses, accreditation etc. It was the expressed wish of this National Commission that similar state committees be set up to discuss these and other important subjects pertaining to patient care. Dr. Bonnet, therefore, representing the Massachusetts Hospital Association, requested the President of the Massachusetts Medical Society to establish such a committee and invite the Massachusetts Nurses Association and the Massachusetts Hospital Association to name representatives.

Five meetings of this committee have been held during the past year. These meetings have shown the value of frank, sometimes acrimonious, interdepartmental discussion, and have resulted in increasing understanding of each others' problems by the nurses, hospital administrators and physicians. At first, as had been done by the national commission, nursing problems were discussed: Why are there too few nurses? What is the nurses' real function? Does it include the psychological aspects of patient care? Is health instruction for patients and their families part of this function? Can and should these subjects be taught to girls in training? It was brought out that the nurse very often has to fill the gaps left vacant by the physician. Too often the doctor's over-all plan (if any!) for the care of the individual patient is never known to the nursing or the dietary staff. If the physician would communicate to the head nurse the diagnosis and his plan of attack (would really function as captain of a team) greater efficiency and understanding would result. The doctors on the committee replied that too often the nurse was unavailable, or too busy making up reports or counting sheets and so forth. The doctors felt the nurses' proper function was to take care of the physical needs of the sick person, and to leave "psychology" alone. The nurses replied that since the doctor frequently failed to give more than specific therapy someone (and often the nurse) must tend to the patients' and families' social needs. Provided she understood what the doctor wanted (so seldom the case), the nurse would supplement his care, or if requested, limit herself to the purely physiologic aspects.

It seemed to the Committee that what was needed here was *communication*, that in each hospital better co-operative care could be achieved if better communication could be established between doctors, nurses and administration. The Committee felt, moreover, that the limits of responsibility of the doctors and nursing groups needed discussion and clarification.

The Committee then strove, not entirely successfully, to deal with the question: What is *essential* in the general care of the patient? It was recognized that this varied with the type of case, the size of the hospital and the general situation. Essential care, during mass bombing, would be very different from that in peacetime.

The Committee finally decided that safety, comfort (including control of noise) and nutrition were the only factors that could be labeled "essential" in the general care of the patient. There was some discussion of appearance and cleanliness of rooms: "patients are unable to judge the medical care they are receiving so they judge the hospital by the things they know, i. e. dust, food and so forth."

One whole meeting was devoted to nutrition and two dietitians were invited guests. It was discovered that in some hospitals over 60 per cent of patients were on special diets by doctor's orders, and one half of these were "salt-free" diets. The Committee felt that the growing tendency to order special diets needed re-examination. This problem again emphasizes the responsibility of the physician by whose order all diets are given.

After long discussion, the Committee agreed that a selective diet was often more economical and usually more satisfactory to the patient than a "standard" diet. The Committee moreover felt that meals should have priority over other services, such as dressings, laboratory tests, examinations and so forth, but emphasized that only by understanding and co-operative planning by the three professional groups could this be achieved.

Routine orders took up another meeting. It was the unanimous feeling that routine orders were generally undesirable, as they often necessitated unnecessary maneuvers (preoperative enemas, the giving of laxatives, daily baths, wheel-chair transportation of ambulatory patients and so forth). In addition, they often resulted in formalized and less intelligent treatment on the doctor's part. The Committee felt also that routine orders lessened the teaching value of the hospital to residents and interns.

The Committee early recognized that healthy and valuable as its discussions proved to be, it was actually talking in a vacuum, with no action at the state level possible. What was needed, the Committee felt, were similar arguments and discussions between the three groups *in each hospital*. The hospital and nursing representatives questioned the doctor's willingness to find the time for this. One Committee member said, "The doctor group is always trying to tell you what to do but they don't come around (to meetings) at all." When a group meeting was called apparently the nurses and hospital administrators appeared, but rarely the doctors. The Committee recognizes and wishes to emphasize that significant improvements can develop only with the *active participation of doctors*. The job cannot be done by nurses and administrators to, or for, doctors. It can only be done *with the doctors*.

The Committee was, however, confident that the doctors were fundamentally interested in any move that would improve the care of the patient; and that they would gladly serve on a hospital committee to work out mutual problems with the nursing staff and hospital administration if they could be convinced that such committee work would bring results. Time and patience are required, however, before results can be shown.

To this end, the Committee has invited twelve Massachusetts hospitals to form trial interdepartmental committees. The Committee is requesting periodic reports from these hospitals, and stands ready to help with advice or suggestions. It is the conviction of the Committee that improvement in patient-care will result from the better understanding between doctors, nurses and administrators that can be achieved by discussion in committee at the local hospital level.

DEATHS

MANARY — James W. Manary, M.D., of Boston, died on September 15. He was in his seventy-first year.

Dr. Manary received his degree from Tufts College Medical School in 1908. He was a fellow of the American College of Hospital Administrators and, formerly, superintendent of the Boston City Hospital.

He is survived by his widow.

NELSON — William A. Nelson, M.D., of Williamstown, died on September 10. He was in his seventy-seventh year.

Dr. Nelson received his degree from Baltimore Medical College in 1904. He was formerly a member of the Williamstown board of health.

He is survived by his widow, a daughter, a son and a sister.

STERN — David Stern, M.D., of Brookline, died on September 15. He was in his fifty-fourth year.

Dr. Stern received his degree from Harvard Medical School in 1926. He was a member of the staffs of the Beth Israel and Boston City hospitals, and a fellow of the American Medical Association.

He is survived by his widow, two daughters, two sisters and two brothers.

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PUBLISHED IN ACCORDANCE WITH THE PROVISIONS OF CHAPTER V, SECTION 2, OF THE BY-LAWS

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University of Vermont College of Medicine, 1953.
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Tufts College Medical School, 1947.

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Harvard Medical School, 1950.

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Harvard Medical School, 1950.

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New York University College of Medicine, 1948.

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Boston University School of Medicine, 1947.

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Boston University School of Medicine, 1953.

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Albany Medical College, 1951.

MAHER, RICHARD JOHN, 337 Appleton St., Holyoke.
Tufts College Medical School, 1949.

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Boston University School of Medicine, 1939.

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George Washington University School of Medicine, 1945. (Transfer from the Medical Society of the District of Columbia.)

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Boston University School of Medicine, 1950.
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Temple University School of Medicine, 1947.
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College of Physicians & Surgeons, Kansas City, 1940.
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CIVIL DEFENSE AGENCY

A CRITICAL ANALYSIS OF THE MEDICAL PROBLEMS OF THREE RECENT MAJOR DISASTERS

No one tome could ever adequately portray the extent of the widespread havoc caused by 3 of the greatest storms ever to strike New England. The Worcester tornado of June 9, 1953, and the hurricanes of August 31 and September 11, 1954, will be long remembered. Since more than 51 tornadoes and several hurricanes have been counted in New England since 1775, recent experience is of significance for future guidance and planning.

Table 1 indicates in a general way the frequency and extent of major disasters in New England in recent years.

TABLE 1. *Major New England Disasters.*

DISASTER	FATALITIES	CASUALTIES HOSPITALIZED	MAJOR INJURIES	MINOR INJURIES	INJURED
Hurricane—1938	494	—	—	—	708
Cocoanut Grove fire, Boston—1942	492	200	—	—	—
Hurricane—1944	47	—	—	—	382
Worcester tornado—1953	90	570	438	867	—
Hurricanes—1954	27	59	28	326	—

The tornado and the hurricanes required many of the hospitals in Massachusetts to mobilize immediately and implement their planning for disaster. They successfully mobilized their personnel, facilities and equipment to care for many thousands of casualties.

Successful mobilization of a hospital to combat any disaster such as a hurricane or tornado can only be accomplished by previous detailed comprehensive planning. The great progress that the science of medicine and surgery has made toward establishing expert mass care of casualties is worthy of note. However, hospital organization and planning must emulate the achievements of physicians and surgeons in the wards and operating rooms. The advances in the scientific fields must be sustained and supported by enlightened organizational planning in equally important fields, in some of which much must still be achieved.

Specifically, the following points could be taken into consideration:

1. Provision of substitute or emergency sources of utilities to aid the physician:
   a. Electricity
   b. Heat
   c. Water
   d. Gas and refrigeration

The importance of the provision of auxiliary power cannot be overstressed, and in hospitals where plans for such power are nonexistent steps should be taken to include this all-important item in future budgets. It is indicative of unrealistic planning when a hospital is entirely incapacitated by a storm that causes a failure of power and thus renders the hospital nonoperative.

2. Plans for the expansion of existing hospital facilities and services to care for a sudden influx of large numbers of casualties, to include:
   a. Locating space within the hospital for litters and cots.
   b. Locating space in vicinity of hospital for litters, cots and related services.
   c. Expansion of nursing services by reassignment of nurses to provide wider coverage (increase of staff would be accomplished through judicious use of nurses' aides and volunteers).
   d. An increase in operating room and related services to care for the large number of casualties requiring immediate surgery.

TABLE 2. *Injuries Sustained among Patients Hospitalized in the Worcester Tornado of 1953.*

DIAGNOSIS	NO. OF CASES
Fractured skull	77
Fractured arm	46
Fractured leg	42
Fractured jaw	2
Eye injury	28
Fractured nose	4
Fractured shoulder & clavicle	21
Fractured pelvis	10
Fractured ribs	32
Fractured back & other back injury	13
Fractured neck	3
Fractured hip	5
Kidney injury	9
Ruptured spleen	6
Burns	5
Lacerations, cuts & contusions	147

The frequency and type of fracture sustained in a tornado disaster are noteworthy (Table 2).

   e. Expansion of central supply to support these services.
   f. Expansion of laboratory, radiology, pharmacy and other departments to support these services.
   g. Expansion of blood bank for increased bleeding operations (many casualties may require treatment for shock; if possible the blood-bank activities should be located away from clinical services for casualties).
   h. Expansion of dietary services to provide food for casualties and personnel—reorganization may include the provision of easily prepared, nutritious meals and additional hours for food service.
3. Development of a personnel pool for disaster conditions:
   a. The need for assistance by both professional personnel and auxiliary workers will be far in excess of that which can be provided by the present hospital staff. Reduction in routine and nonessential procedures and extension of hours of duty will be of considerable assistance. A large number of volunteers will be needed to meet hospital requirements. The personnel pool should include volunteers recruited from local and supporting areas.
   b. The personnel pool should be located suitably convenient to the hospital.
   c. All requisitions for personnel to supplement hospital staff should be made through this pool.

d. Volunteers recruited before a disaster should receive indoctrination and training in their assignments.

In the tornado and hurricanes certain locations suffered extensive damage and consequent loss of life and casualties whereas others received only minor damage. It is realistic and philanthropic planning for every hospital, regardless of location, to have available a nucleus of professional and technical staff that can be dispatched to any large-scale disaster area immediately on request. This important phase of predisaster planning should not be neglected because when any large-scale disaster strikes, loss of life may be averted by avoidance of undue delay.

4. A plan designed to maintain a current disaster organization:
   a. All hospital personnel should be periodically oriented in the details of the hospital disaster plan —that is, at staff and other group conferences.
   b. Efficiency of the disaster organization can be enhanced by periodic maneuvers and drills involving all hospital personnel.

The disasters that have been enumerated indicate the vital need for periodic drills and exercises.

In the tornado and hurricanes widespread disruption of power facilities occurred, with consequent spoilage of large quantities of food in cold storage. Measures of public-health significance were taken to prevent ill effects. Likewise, foodstuffs and water supplies were contaminated because of flooding and backward seepage of sewage. The necessary preventive measures were taken. No cases of illness were reported.

Although rescue, transportation, evacuation and triage of casualties presented their own special medical problems during the tornado and hurricane disaster operations, it is not within the general scope of this paper to consider them.

THOMAS F. MAHER, M.D., D.P.H.
Executive Medical Officer

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CORRESPONDENCE

OBSTETRIC ANXIETY

To the Editor: The letter from Dr. Archie A. Abrams in the August 19 issue of the *Journal* regarding the new mother's anxiety over engaging a practical nurse brings to mind the difficulties the pediatrician encounters in dealing with these paragons once they are on the job. How much of the physician's time must be spent in trying to revise the nurse's ideas on feeding a particular infant while bolstering the mother's ego so that she will eventually feel adequate to care for her own baby!

The obstetrician can do much to reassure the healthy pregnant woman that she is capable of mothering her own child at home with housekeeping assistance for a short period from a person who does not presume to be a "nurse." The insecurities of many prospective mothers might be reduced by the realistic experience of helping out a friend with several young children for a few afternoons.

In this era of the "baby sitter," perhaps adolescents will learn, while baby tending, a more relaxed attitude toward children that will later help them with their own offspring.

LAWRENCE S. MORSE, M.D.
Boston

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR AUGUST, 1954

RÉSUMÉ

DISEASE	AUGUST 1954	AUGUST 1953	SEVEN-YEAR MEDIAN
Chancroid	2	3	1
Chicken pox	121	116	179
Diphtheria	1	3	7
Dog bite	1525	1054	1196
Dysentery, bacillary	15	92	7
Encephalitis, infectious	3	2	2
German measles	74	56	63
Gonorrhea	181	268	260
Granuloma inguinale	0	0	0
Hepatitis, infectious	87	55	91†
Lymphogranuloma venereum	1	3	1
Malaria	2	0	1
Measles	708	41	151
Meningitis, meningococcal	5	1	3
Meningitis, Pfeiffer bacillus	2	0	1
Meningitis, pneumococcal	0	0	0
Meningitis, staphylococcal	0	0	0
Meningitis, streptococcal	0	1	1
Meningitis, undetermined	5	3	3
Mumps	455	342	275
Poliomyelitis	234	109	97
Salmonellosis	33	28	12
Scarlet fever	80*	55	55
Syphilis	135	198	166
Trichinosis	2	3	3
Tuberculosis, pulmonary	247	147	181
Tuberculosis, other forms	6	10	10
Typhoid fever	3	1	3
Undulant fever	1	0	2
Whooping cough	159	166	209

*Includes streptococcal sore throat.
†Five-year median.

COMMENT

Diseases below the seven-year median were chicken pox, diphtheria and whooping cough.

Diphtheria continued to be on the wane. Only one case was reported during the month of August. This brings the total for the year so far to only 19.

The diseases above the seven-year median were bacillary dysentery, German measles, infectious hepatitis, measles, mumps, poliomyelitis, salmonellosis and scarlet fever.

Bacillary dysentery, though somewhat higher during August than the seven-year median, showed, nevertheless, a marked reduction in incidence from the high point reached in the summer of 1953. This high level was sustained through the end of the winter.

Salmonellosis, on the other hand, showed no tendency to decline but maintained a rather high incidence.

The increased incidence of measles during August was not unexpected since last year was the low point in the state's history.

Poliomyelitis was higher during August this year than the corresponding month in recent years with the exception of the peak year 1949. A high proportion of nonparalytic cases may mean that other viruses may have caused symptoms that resembled poliomyelitis.

Geographical Distribution of Certain Diseases

The following diseases were reported from the communities named:

Diphtheria: Cambridge, 1; total, 1.

Dysentery, bacillary: Attleboro, 1; Danvers, 4; Tewksbury, 9; Wenham, 1; total, 15.

Encephalitis, infectious: Cambridge, 1; Lancaster, 1; South Hadley, 1; total, 3.

Hepatitis, infectious: Boston, 9; Brockton, 2; Cambridge, 4; Chelsea Naval Hospital, 2; Fall River, 17; Falmouth, 1; Fort Devens, 1; Haverhill, 2; Hull, 1; Lexington, 1; Lowell, 8; Lynn, 5; Melrose, 1; Milford, 2; Needham, 1; North Adams, 3; Pittsfield, 2; Plymouth, 1; Quincy, 1; Revere, 1; Shrewsbury, 1; Somerville, 1; Southwick, 2; Springfield, 1; Taunton, 1; Waltham, 2; Ware, 1; West Bridgewater, 1; Williamstown, 1; Worcester, 6; Wrentham, 5; total, 87.

Lymphocytic choriomeningitis: Chicopee, 1; total, 1.

Malaria: Fort Devens, 2; total, 2.

Meningitis, meningococcal: Boston, 2; Paxton, 1; total, 3.

Meningitis, Pfeiffer bacillus: Beverly, 1; Reading, 1; total, 2.

Meningitis, mumps: Lancaster, 1; Newton, 1; Watertown, 1; total, 3.

Meningitis, undetermined: Dalton, 1; Fall River, 1; Salem, 1; Somerville, 1; Springfield, 1; total, 5.

Poliomyelitis: Arlington, 4; Attleboro, 6; Auburn, 4; Beverly, 4; Boston, 31; Braintree, 4; Brockton, 2; Brookline, 2; Cambridge, 3; Charlton, 1; Chelsea, 3; Concord, 1; Danvers, 4; Dracut, 1; Everett, 2; Fall River, 3; Fitchburg, 3; Framingham, 1; Franklin, 1; Grafton, 1; Greenfield, 1; Harvard, 1; Haverhill, 8; Holden, 1; Hull, 1; Lakeville, 1; Lawrence, 1; Lexington, 2; Leicester, 1; Lowell, 3; Lynn, 3; Malden, 3; Mansfield, 2; Marblehead, 1; Mattapoisett, 1; Medford, 5; Mendon, 1; Methuen, 1; Middleboro, 2; Milford, 1; Millbury, 2; Nantucket, 1; Natick, 1; Newburyport, 1; Northbridge, 3; Oxford, 3; Peabody, 1; Pittsfield, 4; Plymouth, 2; Quincy, 9; Reading, 1; Rehoboth, 1; Revere, 8; Salem, 4; Scituate, 1; Shrewsbury, 3; Somerville, 1; Southbridge, 1; Springfield, 3; Stockbridge, 1; Stoughton, 1; Sturbridge, 1; Tewksbury, 2; Upton, 3; Waltham, 3; Watertown, 1; Wayland, 1; Webster, 2; Wellesley, 1; Westport, 1; Weymouth, 3; Whitman, 1; Winchendon, 2; Woburn, 3; Worcester, 37; total, 234.

Psittacosis: Holbrook, 1; total, 1.

Salmonellosis: Attleboro, 1; Boston, 2; Braintree, 1; Cambridge, 5; Essex, 1; Everett, 1; Haverhill, 3; Holden, 1; Lawrence, 3; Lowell, 2; Malden, 1; Medford, 1; Melrose, 1; Pittsfield, 2; Plymouth, 1; Somerville, 1; Tewksbury, 1; Wakefield, 2; Wenham, 1; Westfield, 1; Worcester, 1; total, 33.

Tetanus: Somerville, 1; total, 1.

Trichinosis: Falmouth, 1; Quincy, 1; total, 2.

Typhoid fever: Amesbury, 1; Haverhill, 1; New Bedford, 1; total, 3.

Undulant fever: Ipswich, 1; total, 1.

NONCLINICAL NOTES

INTERNATIONAL SOCIETY OF CARDIOLOGY

Dr. Paul D. White, of Boston, has been elected president of the International Society of Cardiology. He succeeds Professor Charles Laubry.

NOTICES

MASSACHUSETTS SOCIETY FOR RESEARCH IN PSYCHIATRY

The meetings of the Massachusetts Society for Research in Psychiatry will be as follows: October 27, December 1, February 4 and April 8.

MASSACHUSETTS ASSOCIATION OF MEDICAL TECHNOLOGISTS

The semiannual meeting of the Massachusetts Association of Medical Technologists will be held at the Beverly Hospital, October 30, starting at 9:30 a.m. The program is as follows:

Administrative Aspects of Blood Banking. Dr. Donald Brown.

Use of Separated Red Blood Cells and Plastic Equipment. Dr. John G. Gibson, II.

Problem of the Du. Dr. Alan R. Jones.

Blood-Group Serology and Its Practical Aspects in Blood-Transfusion Work. Dr. Morten Grove-Rasmussen.

Afibrinogenemia. Dr. Luke Gillespie.

Pancreatic-Function Tests. Dr. Harry Shwachman.

CONFERENCE ON ATOMIC OPPORTUNITIES

A conference on atomic opportunities in New England sponsored by the New England Council and the Atomic Industrial Forum will be held at the Hotel Statler on October 20, starting at 10 a.m. Dr. Shields Warren will preside at the medical session.

EDWARD K. DUNHAM LECTURES

The Edward K. Dunham lectures will be presented by Professor Konrad Z. Lorenz, departmental director, Max-Planck-Institute für Verhaltensphysiologie Schloss Buldern über Dülmen, Westfalen, Germany, on the topic "Approach to Behavior Study from the Viewpoint of Comparative Phylogenetics" in the amphitheater of Building C, Harvard Medical School, 25 Shattuck Street, Boston, at 5 p.m. on the following dates:

October 25. Innate Motor Patterns.
October 27. Innate Releasing Mechanisms.
October 29. The Organization of Innate Behavior.

A fourth lecture will be presented under the auspices of the departments of Biology and Psychology, Harvard University, on the subject "Problems of Expression Movements and Ritualization" in Room 18, Geographical Institute, 2 Divinity Avenue, Cambridge, on November 1 at 5 p.m.

MASSACHUSETTS SOCIETY OF EXAMINING PHYSICIANS

The fall dinner meeting of the Massachusetts Society of Examining Physicians will be held at the Harvard Club of Boston on Wednesday, October 27. The social hour will be at 6 p.m., and the dinner at 7. After the dinner there will be a symposium on peripheral vascular disease. The panel of speakers for the meeting will consist of Dr. Richard Warren (moderator), associate visiting surgeon, Massachusetts General Hospital, and consultant in vascular diseases at the Veterans Administration Hospital in West Roxbury; Dr. Edward A. Edwards, staff member, Peter Bent Brigham Hospital, and consultant in vascular diseases, Robert Breck Brigham Hospital; Dr. Robert R. Linton, visiting surgeon and chairman of the Peripheral Vascular Clinic at the Massachusetts General Hospital; and Dr. Everett O'Neil, surgeon-in-chief of a surgical service at the Boston City Hospital.

All interested physicians are cordially invited to attend the meeting and take part in the discussion.

SOCIETY MEETINGS AND CONFERENCES

October, 1954–April, 1955. Postgraduate Medical Institute. Page 451, issue of September 9.
October 16–22. American Occupational Therapy Association. Page 1092, issue of June 24.
October 18–December 8. Postgraduate Seminar in Psychiatry and Neurology. Page 452, issue of September 9.
October 18 and 19. American Cancer Society. Page 631, issue of October 7.
October 18, 1954–January 17, 1955. Hartford Medical Society. Page 496, issue of September 16.
October 18–29. New York Academy of Medicine Graduate Fortnight. Page 44, issue of July 1.
October 19. South End Medical Club. Page 631, issue of October 7.
October 19–28. Consultation Clinics for Crippled Children in Massachusetts. Page 586, issue of September 30.
October 20. Conference on Atomic Opportunities. Notice above.
October 22. National Vitamin Foundation Symposium. Page 410, issue of September 2.
October 22 and 23. American Trudeau Society (Eastern Section). Page 544, issue of September 23.
October 25. Massachusetts Heart Association Kidney Section. Page 631, issue of October 7.
October 25–27. New England Postgraduate Assembly. Hotel Statler, Boston. Page X, Advertising Section.
October 25–27. National Gastroenterological Association. Page 496, issue of September 16.

OCTOBER 25, 27 and 29. Edward K. Dunham Lectures. Page 679.
OCTOBER 25–30. Course in Care of Atomic Casualties. Page 285, issue of August 12.
OCTOBER 27. Massachusetts Society of Examining Physicians. Page 679.
OCTOBER 27. New England Obstetrical and Gynecological Society. Annual Meeting. Hotel Somerset, Boston.
OCTOBER 27–29. International Symposium on the Hypophyseal Growth Hormone. Page 1092, issue of June 24.
OCTOBER 27, DECEMBER 1, FEBRUARY 4 and APRIL 8. Massachusetts Society for Research in Psychiatry. Page 679.
OCTOBER 29. Massachusetts Public Health Association. Fall Meeting. Blake's Restaurant, Springfield, Massachusetts.
OCTOBER 30. Massachusetts Association of Medical Technologists. Page 679.
OCTOBER 31. Medical Television Program. March of Medicine. Page 631, issue of October 7.
OCTOBER 31–NOVEMBER 4. American Institute of Dental Medicine. Page 968, issue of June 3.
NOVEMBER, 1954–MAY, 1955. Sanitary Engineering Center Training Programs. Page 122, issue of July 15.
NOVEMBER 2–5. Fourth Annual Bay State Rehabilitation Conference. Hotel Statler, Boston.
NOVEMBER 2–6. National Society for Crippled Children and Adults. Page 631, issue of October 7.
NOVEMBER 3 and 4. M & R Pediatric Research Conference. Page 496, issue of September 16.
NOVEMBER 6. Massachusetts Hospital School Symposium. Page 495, issue of September 16.
NOVEMBER 12. Memorial Center for Cancer and Allied Diseases Conference. Page 544, issue of September 23.
NOVEMBER 12 and 13. Inter-Society Cytology Council. Page 968, issue of June 3.
NOVEMBER 15–19. American College of Surgeons. Page 496, issue of September 16.
NOVEMBER 15–26. Laboratory Diagnosis of Tuberculosis Course. Page 246, issue of August 5.

CALENDAR FOR THE WEEK BEGINNING THURSDAY, OCTOBER 21

THURSDAY, OCTOBER 21
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:00–10:00 a.m. Combined Medical-Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.
*9:00–10:00 a.m. Arthritis Grand Rounds. Robert Breck Brigham Hospital.
*10:00–11:00 a.m. Medical Staff Conference. Sherman Auditorium, Beth Israel Hospital.
*10:00–11:00 a.m. Surgical Rounds. 5th floor teaching unit, Beth Israel Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m. Thoracic Conference. Pulmonary Function Studies. Dr. Warren J. Taylor. Main Amphitheater, Peter Bent Brigham Hospital.
*11:00 a.m.–12:30 p.m. Hand Clinic (Physical Medicine and Rehabilitation Service). Boston City Hospital.
*12:00 m.–1:00 p.m. The Agents of Varicella and Herpes Zoster. Dr. Thomas H. Weller. Stearns Auditorium, New England Center Hospital.
*4:00–5:00 p.m. Pediatric Seminar. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.

FRIDAY, OCTOBER 22
American Trudeau Society. Eastern Section. Sheraton Hotel, Washington, D. C.
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:30–11:30 a.m. Medical and Surgical Grand Rounds. Drs. George W. Thorn and Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.
*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit, 57 East Concord Street.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m. Mortality and Morbidity Meeting. Dr. A. Bova. St. Margaret's Hospital, Dorchester.
*11:00 a.m.–1:00 p.m. Medical Grand Rounds. Dr. Proger and Staff. Stearns Auditorium, New England Center Hospital.
*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.
*1:30 p.m. Tumor Clinic. Mount Auburn Hospital, Cambridge.
*4:00–5:00 p.m. Child Psychiatry. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.
*4:00–6:00 p.m. X-Ray Conference. Dr. Merrill Sosman. Stearns Auditorium, New England Center Hospital.
*4:00–10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Waltham Street.

SATURDAY, OCTOBER 23
American Trudeau Society. Eastern Section. Sheraton Hotel, Washington, D. C.
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Anesthesia Conference. Dr. Etsten. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*8:30–10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.
*9:00–10:30 a.m. Surgical Grand Rounds. Dr. Child and Staff. Stearns Auditorium, New England Center Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:00 m. Hematology Clinic. Dr. William Dameshek. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.

MONDAY, OCTOBER 25
New England Postgraduate Assembly. Hotel Statler, Boston.
National Gastroenterological Association. Shoreham and Walter Reed Army Medical Center Hospital, Washington, D. C.
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Medical and Surgical Clinic on Diabetic Problems. New England Deaconess Hospital.
*8:30–9:30 a.m. Clinic by entire Surgical Staff and Anesthesia Staff. Cheever Amphitheater, Dowling Building, Boston City Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*12:00 m.–1:00 p.m. Medico-Pathologic Conference. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*4:00 p.m. Clinicopathological Conference. Pathology Conference Room, Beth Israel Hospital.
*4:00–5:00 p.m. Surgical Pathology. Dr. MacMahon. Stearns Auditorium, New England Center Hospital.
5:00 p.m. Edward K. Dunham Lecture. Building C, Harvard Medical School, 25 Shattuck Street.
*5:00–6:30 p.m. Anesthesia Group of the Lahey Clinic. Joslin Auditorium, New England Deaconess Hospital.
5:15 p.m. Staff Meeting. Harris Hall, New England Deaconess Hospital.
*7:00–8:00 p.m. Pathology Conference. Dr. MacMahon and staff. Stearns Auditorium, New England Center Hospital.
*8:00 p.m. Massachusetts Heart Association Kidney Section. Morse Auditorium, Museum of Science, Science Park, Boston.

TUESDAY, OCTOBER 26
New England Postgraduate Assembly. Hotel Statler, Boston.
National Gastroenterological Association. Shoreham and Walter Reed Army Medical Center Hospital, Washington, D. C.
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:00 a.m. Geriatrics Clinic. Peter Bent Brigham Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*12:00 m. Pediatric Grand Rounds. Cheever Amphitheater, Dowling Building, Boston City Hospital.
*12:00 m.–1:00 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.
12:00 m.–1:00 p.m. Endocrine Conference. Dr. Astwood. Stearns Auditorium, New England Center Hospital.
*12:15–1:15 p.m. X-Ray Conference. Dr. Merrill Sosman. Main Amphitheater, Peter Bent Brigham Hospital.
12:30–1:30 p.m. Medical Journal Club. Joslin Clinic, New England Deaconess Hospital.
*4:00–5:30 p.m. Anesthesia Conference. Dr. Etsten. Stearns Auditorium, New England Center Hospital.
*5:00 p.m. Surgical Journal Review. Mount Auburn Hospital, Cambridge.
*5:00–6:00 p.m. Service Meeting Followed by Clinical Conference (Medical, Surgical, Obstetrical). Faulkner Hospital.
*5:00–6:00 p.m. Clinical and X-Ray Pelvimetry. Dr. D. McSweeney. St. Margaret's Hospital, Dorchester.

WEDNESDAY, OCTOBER 27
New England Postgraduate Assembly. Hotel Statler, Boston.
National Gastroenterological Association. Shoreham and Walter Reed Army Medical Center, Washington, D. C.
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m. Orthopedic Grand Rounds. Bigelow Amphitheater, White 4, Massachusetts General Hospital.
*11:00 a.m. Boston State Hospital Psychiatric Seminar. Reception Building Auditorium, 591 Morton Street, Dorchester.
*12:00 m.–1:00 p.m. Clinicopathological Conference. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*12:00 m.–1:00 p.m. Neurology, Neurosurgery and Psychiatry Conference. Drs. Sullivan, B. Selverstone and Hope. Stearns Auditorium, New England Center Hospital.
*12:00 m.–1:00 p.m. Roentgen Diagnostic Conference. 5th floor teaching unit, Beth Israel Hospital.
*12:30 p.m. Weekly Pathological Meeting. Joslin Auditorium, New England Deaconess Hospital.
*12:30–1:30 p.m. Weekly Staff Review of Autopsies. Dr. William A. Meissner. Joslin Auditorium, New England Deaconess Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*1:00 p.m. Massachusetts General Hospital Hand Clinic. Out-Patient Department.
*2:00 p.m. Rectal Clinic. Peter Bent Brigham Hospital.
*2:00–3:00 p.m. Pediatric Conference for Practitioners. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*4:00–5:30 p.m. Fracture Lecture. Boston City Hospital.
*4:00–6:00 p.m. Overholt Thoracic Conference. Joslin Auditorium, New England Deaconess Hospital.
5:00 p.m. Edward K. Dunham Lecture. Building C, Harvard Medical School, 25 Shattuck Street.
*6:00 p.m. Massachusetts Society of Examining Physicians. Harvard Club of Boston.
*6:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*7:00–9:00 p.m. Postgraduate Seminar in Pediatric Neurology and Psychiatry. Walter E. Fernald State School, Waltham.
*7:30–9:30 p.m. Lahey Clinic Lecture. Joslin Auditorium, New England Deaconess Hospital.

*Open to the medical profession.